

**Synthesising Heterogeneity:  
trends of visibility in biological sciences circa 1970s - 2000s**

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## Abstract

This is a case study of diagrams in a field of biological mechanism research (apoptosis), revealing that mechanism diagrams play a crucial role in the practice of developing mechanistic explanations for cell biology.

This thesis supports and extends the existing literature in the following aspects: the relationship between scientific representation and practice (Daston and Galison, 2007), inter-field and inter-level integration in biological practice of mechanism research (Bechtel, 2006; Craver and Darden, 2013), and the assertive and engaging power of diagrams (Bender and Marrinan, 2010; Wood, 1992, 2010).

The methodology is composed of two parts: quantitative and qualitative. The quantification draws the comprehensive patterns of diagram use via analysing the coverage of diagrams. The qualitative part analyses three layers of the diagrams: visual element, composition, and style. This part contextualises the diagrams in four senses: source of ideas, perspective, adjacent text, scope of research.

The results and the interpretation of results are also composed of quantitative and qualitative parts. The quantitative part shows a noticeable prevalence of two themes of diagrams: object and mechanism. The former reflects an interest in manipulating entities. The latter reflects an interest in integration of, and interaction between, different perspectives. The relative changes in the coverage of these two themes suggest a shift in the focus of practice from manipulation of biological entities toward inter-field interaction between heterogeneous perspectives.

The qualitative part contains a central argument and several interesting discoveries. The central argument is that mechanism diagrams synthesise heterogeneity and thus have the power to assert novel ideas and engage real-world practice. The heterogeneity of perspectives is embedded in the practice of developing the cell models. The term “synthesis” means that novel meanings emerge from the integration of existing perspectives. This novelty of meanings attributes to the assertive power of mechanism diagrams. The engaging power facilitates interaction amongst the component perspectives, which is an important feature of mechanism research. In sum, this argument can explain the increasing reliance upon diagrams found in the quantitative results.

The other interesting qualitative discoveries include but are not limited to the following. Firstly, biological diagrams can go beyond visual resemblance to entities. Secondly, there are many creative ways of making diagrams, such as importing visual vocabulary from non-specialist areas and modular use of visual elements. These creative ways show that visual conventions in biological diagrams are not given but undergo evolution, probably responding to the growing complexity of ideas. Thirdly, the evolution of biological visualisation is not merely driven by development of technology but embodies the interaction between ideas and technological advancement.

The conclusion of this study treats mechanism diagrams as both epistemological and communicative devices acting in the research dynamics. The communication is part of the processes of knowing and intervening, taking place both horizontally and longitudinally. The horizontal communication is amongst different research groups in the field. The longitudinal communication is between different stages of model developing by the same individuals. Diagrams serve in the constant defining and redefining of boundary of research arenas through bringing about new problems and activating future research.



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## **Figures**

Figures in this thesis are presented separately in Volume II in numerical sequence.

# Chapter One: Introduction

## 1.1 Introduction

Diagrams have a massive presence in biological literature. This thesis explores the patterns of visual representation in contemporary biological sciences by surveying and analysing the journal diagrams in the apoptosis research field between circa 1970 and 2005. By doing so, this thesis reveals the interplay between visual culture and biological practice.

This study fills three gaps in the existing literature. Firstly, it provides the first systematic survey of contemporary biological visualisation. Secondly, this study employs a novel combination of quantitative and qualitative methods. Such an approach covers both the comprehensive patterns of visual practice and an in-depth analysis of the complex contents of diagrams. Thirdly, this study specialises in mechanism diagrams, arguing that they are epistemic and communicative vehicles for constructing mechanistic cell models. Before this study, this philosophical idea had not been supported by an analysis at this scale.

Visual objects in different sciences have attracted attention of both historians and sociologists since the late 1980s<sup>1</sup>. These studies have shown the intimate link between scientific practice and visual representation, as well as the fact that certain scientific values can be embodied in visual objects<sup>2</sup>. Nevertheless, this thesis identified three gaps in the existing literature: lack of large systematic studies, limited discussion on novel features of contemporary biological visuals, and lack of analysis of the relationship between visual representation and practice in biological mechanism research. Below I explain each point.

Firstly, there is a need for empirical studies on large populations of images. Studies of the visual culture in science tend to focus on single, elegant examples. This study complements the existing literature through a large-scale survey, covering eight journals across roughly three decades. The aim is to study a representative population of the field and provide a meaningful interpretation of the patterns.

Secondly, contemporary biological visualisation requires deeper insights in the way practitioners treat them. Few sources have covered biological visualisation from the late twentieth century onward, as most of the existing studies on biological and medical visualisations focus on illustrations before the middle twentieth century<sup>3</sup>. For biological visualisation from the late twentieth century onward, scholars generally focus on either the impact of novel technologies or the social interactions in laboratory practice<sup>4</sup>. Such existing literature tends to treat contemporary biological images in a mixed way<sup>5</sup>. Namely, different kinds of visuals (eg. photographs, graphs, diagrams etc.) are not distinguished from one another. However, in biological practice, there normally exists a distinction between data images (generated through experiment and simulation)

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1 For example, see Galison and Jones ed. 1998; Pauwels ed., 2006.

2 Daston and Galison (2007) is a landmark work of this view.

3 For example, see Taylor and Blum (1991), which also nicely introduces the trend of studying scientific visibility at the time.

4 For the impact of novel technologies, see Carusi, 2012; Carusi, Hoel et al. ed., 2014; Coopmans, Vertesi et al. ed., 2014; Laubichler and Müller (2007). More papers can be found in a special issue from the journal *Spontaneous Generations* on “Visual Representation and Science” (2012).

For the social aspect of lab practice, Amann and Knorr Cetina (1988) is a good example.

5 Lynch’s study on biological diagrams is an important exception.

and diagrams (purposefully drawn to model specific ideas). This is to say that biologists convey different kinds of scientific knowledge—and have different intentions—when they use these two different kinds of images. This thesis fills this gap by concentrating on biological diagrams between the 1970s and 2005.

Thirdly, the interplay between visual representation and biological practice in mechanism research requires more attention. Intense philosophical debates have been focusing on mechanisms *per se*<sup>6</sup>. A few historical and philosophical studies have touched the epistemological features of diagrams in developing mechanistic models in biology (see Section 2.4). However, in-depth analyses of the content of diagrams are required to capture the relationship between visual representation and model construction. This is because diagrams in mechanism research serve the biologists both in their achievement and presentation of novel ideas. An in-depth analysis will reveal *both* the epistemic and communicative roles of diagrams play in developing mechanistic cell models.

This study shall confirm two crucial functions of diagrams in biological mechanism research: conveying complex ideas and provoking dialogues amongst diverse practices. Based upon the survey of a large sample size, I will argue that these functions result from diagrams synthesising heterogeneous perspectives. The reflective case is the apoptosis field since the late twentieth century, when an increasing need of local perspectives to interact paralleled the growing richness of visual representation.

In the apoptosis field, diagrams (especially those ones representing mechanisms) are the increasingly preferred format of visually contextualising discoveries in existing knowledge. I will argue that this should be due to the epistemic and communicative roles of diagrams. Diagrams embody the culture of biological mechanism research, which requires interaction between and integration of multiple perspectives for the same phenomena. The development of cell models tends to be intertwined with the development of diagrams, both in epistemological and social senses. Therefore, I will conclude that mechanism diagrams are simultaneously the representations and part of the practice.

## 1.2 The case: apoptosis

The case study is apoptosis. It is chosen for two reasons. Firstly, it is typical of biomedical practice. Secondly, it exhibits the key features of biological mechanism research.

Apoptosis plays roles in a very broad range of physiology and pathology. A survey on this field can thus cover various research areas and practices. Apoptosis is also known as “programmed cell death”, when the cell “commits suicide” through specific processes. Nowadays the term “apoptosis” is also used to distinguish between this kind of cell death and necrosis. In the latter situation, the death is accompanied with release of lots of substances causing harm to the neighbouring cells (Alberts et al., 2002, 1011). Apoptosis is a process of “neat” cell death and ends up with phagocytosis by either neighbouring cells or macrophages (2002, 1011). Both intracellular and extracellular “death signals” can induce apoptosis. Once induced, an amplifying cascade of enzymatic activations breaks cellular substances (proteins and DNA), resulting in destruction of normal cell function (2002, 1010-11). In physiological homeostasis, both developmental and adult tissues undergo apoptosis to renew and maintain. Apoptosis is also involved in a myriad of pathological situations, including cancer, Parkinson's disease, and autoimmune diseases.

More importantly, the history of apoptosis becoming scientifically significant has an immediate link with the emergence of mechanistic view for cell phenomena. The rapid growth of apoptosis field

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<sup>6</sup> See Illari and Williamson (2012) for a summary of the debates.

since the late 1980s witnessed and embodied the burgeoning of mechanism-oriented research. This growth paralleled both the proliferation of novel techniques and the differentiation of research areas. While both apoptosis and necrosis had been observed in the nineteenth century, and while the morphology of apoptosis has been studied with the aid of electron microscopy in the early 1970s<sup>7</sup>, apoptosis had not come into the limelight until the end of the 1980s<sup>8</sup>. The lack of wide spread interest in apoptosis before the 1990s is expressed in the *Preface* to a 1994 volume of *Cold Spring Harbor Current Communications in Cell and Molecular Biology*:

When these projects [of books on apoptosis] were first conceived in 1990, the word *apoptosis* was not a commonly recognized term – much less a widely accepted scientific idea. At that time, as much concern was frequently expressed over the pronunciation of the word as for the scientific implications of the concept. (Tomei and Cope, 1994, vii)

The growth of interest in apoptosis is correlated with a transition from morphological, descriptive to molecular, explanatory, and mechanistic accounts. This transition started around the middle twentieth century and is recognised by the practitioners in different biological fields<sup>9</sup>. But this transition took place relatively late in the apoptosis field. Apoptosis researchers normally consider the identifications of regulatory genes circa the late 1980s to the early 1990s as the breakthroughs<sup>10</sup>. In the philosophical language of mechanism research, the identification of relevant *entities* and *activities* led to the exploding interest in revealing the mechanisms. Also, the development of *explanations* for apoptosis also made it an important topic across various biological disciplines. This is owed to the pragmatic value of applying apoptosis research to intervention in diseases<sup>11</sup>. Then, apoptosis research developed toward a systematic field that invites interactions between local researchers. This development is evidenced in (1) the exponential growth of publications and (2) the rapid increase of research areas that published apoptosis papers<sup>12</sup>. Eventually in the late 1990s, a journal specialising cell death (and related issues on cell cycle) was established, and the specialist societies had been founded<sup>13</sup>. These events responded to the credibility of apoptosis, as it came to be a topic in major biological reviews, such as the *Annual Reviews*<sup>14</sup>. The practitioners explain that the process of apoptosis gaining scientific credit was motivated by a shift of research focus toward mechanistic thinking:

It was not until apoptosis moved from the morphological to the mechanistic that it fully acquired scientific credibility and began to provide an intellectual framework for the previous scattered observations. (Melino and Vaux 2010, 3)<sup>15</sup>

In sum, given the broad coverage of research areas by apoptosis, as well as the close link between apoptosis and the interest in biological mechanisms, this study assumes that examining the images

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- 7 Kerr et al., 1972; Kerr, 2002. Many more reviews and textbooks refer to the landmark study of Kerr et al. as the transition from scattered observations to interpretive investigation. The paper series by Kerr et al. (between the late 1960s and the early 1970s) are also the first one who proposes the term “apoptosis” to refer to the specific kind of cell death.
- 8 For example, see Garfield and Melino, 1997. This delayed recognition effect is mentioned in many review papers on the history of apoptosis research.
- 9 Developmental biology is a good example of this historical shift to molecular and mechanistic views. For example, in Britain, the specialist community had not turned into a “society” from the embryologists’ “club” until the research focus changed to the molecular mechanisms (Slack, 2000).
- 10 For examples, see Tomei and Cope, 1994; Wallach et al., 1997; Song and Steller, 1999; Lockshin and Zakeri, 2001; Vaux, 2002. For examples of the milestones, see Figure 1 of Vaux, 2002.
- 11 Reed and Green, 2011; Tomei and Cope, 1994.
- 12 Garfield and Melino, 1997; Lockshin and Zakeri, 2001.
- 13 The journal *Cell Death and Differentiation* was established in 1997. The *International Cell Death Society* developed from 1995 to 1998, see The International Cell Death Society, 2012.
- 14 Lockshin and Zakeri 2001, 549.
- 15 Evidence of this view can be found by surveying the textbooks. For example, a 1973 textbook *Cell Physiology* (Giese, 1973) does not have contents related to cell death.

in apoptosis research is to shed light on the relationship between the practice and visual representation in biological mechanism research.

### 1.3 Thesis plan

This thesis is structured similarly to a scientific paper. The chapters include a literature review, methodology, results, discussion, and conclusion. For ease of reference, all figures are included in Volume II of this thesis. The design of the thesis structure is in line with the scientific approach of this study. The goal is to firstly highlight the data per se and secondly address my interpretation. A scientific structure offers convenience for drawing a distinction between data presentation and interpretation. Moreover, this structure is intended to be friendly to scientific readers, as this thesis aims to engage the practice with historical and philosophical accounts for it.

Chapter Two reviews important sources that make contributions to my analytical framework. Daston and Galison (2007) show that plural ideas of “right depiction” can be embodied in visual representations and that new images since the late twentieth century have been shifting from evidential representations toward tools for intervention. Rudwick (1976), Ferguson (1977), and Gooding (1990) examine the functions of diagrams as both communicating and thinking tools in different disciplines. These three works are landmark arguments for the independent value of scientific images that is beyond merely aiding the text. Rasmussen (1997) examines the process of mapping between novel and existing knowledge. This thesis imports his account to discuss the features of biological mechanism research reflected in the diagrams. Both Bechtel (2006) and Craver and Darden (2013) specialise the nature of biological mechanism research. Their arguments on the inter-field and inter-level convergence of practices point out the key features of the practice that are reflected by the visual culture, as this study will argue. Then, both Bender and Marrinan (2010) and Wood (1992, 2010) form the art history part of my framework. They argue for three central features of diagrams: heterogeneity of components, synthetic nature of the whole, and the function of engaging both the viewer with real-world action. Finally, Lynch (1990, 2014) offers a starting point for investigating the relationship between the practice and diagrams in biology by arguing for the sophisticated process of rendering diagrams from photographs.

Chapter Three describes my methodology, which is divided into quantitative and qualitative parts. Table 3.1 will present the scale of the survey undertaken for data collection.

Chapter Four presents the results. The quantitative analysis calculates (1) the frequency of diagrams, both overall and of different types, and (2) the proportion of each type in a breakdown by journal and by decade. The taxonomy of diagrams for this study is based on the genre: object, chemical structure, experimental design, mechanism, and other (miscellaneous). The qualitative analysis investigates the contents of the diagrams in terms of visual element, configuration, and style. Each section of Chapter Four reports the results in sequence: firstly, the patterns of frequency and proportion of diagrams in general and of each type are reported. Secondly, typical examples are raised to demonstrate the trend of diagram contents. Thirdly, rare and special cases are discussed. The special cases vary in the way they deviate from the norms, where many of them are about visual experiments.

Chapter Five analyses the results and develops my arguments on the key features of biological diagrams.

Section 5.1 shows that the quantitative results suggest an increasing favour (sometimes significantly) in diagrams in most of the journals surveyed. Most of the journals exhibit a shift of visual focus from descriptive object diagrams to explanatory mechanism diagrams. In journals that do not obviously show this shift due to their scopes, a notable interest in mechanism diagrams is

still observed.

Section 5.2 explores the richness of biological diagrams by arguing that they can serve more than as resemblances of entities. Biological diagrams since the late twentieth century have become more capable of conveying abstract concepts and explaining phenomena.

Section 5.3 discusses visual innovations and contains four noteworthy findings. Section 5.3.1 explores the quasi-modular use of visual elements in different contexts of making diagrams. Section 5.3.2 discusses that non-specialist visual elements are imported and imposed new, professional meanings. Such a remaking of visual language can contribute to the conceptualisation of professional ideas. Section 5.3.3 reveals the plurality of arrow meanings and argues that such versatile functions of arrows are key to conveying the dynamics of mechanisms. However, this plurality sometimes causes confusion even to the expert viewer. Section 5.3.4 centres on an interesting finding: an aesthetic emphasis on the mitochondria in many diagrams. I will suggest two possible explanations.

Section 5.4 reconsiders a common assumption that novel technologies are the main driving force of the evolution of biological visualisation. Section 5.4.1 explores an intriguing relationship between technology and the making of object diagrams. While the aesthetics is enriched and human labour is reserved by novel tools, the very ideas embedded in the drawings are traditional. Section 5.4.2 discusses visual elements and compositions of mechanism diagrams, showing that the growth of complex ideas has a bigger impact on the evolving visualisation than novel technologies do.

Section 5.5 and 5.6 contain the most important components of my arguments by focusing on the mechanism type. These components contain two parts: heterogeneity embedded in mechanism diagrams (Section 5.5) and meaningful synthesis of heterogeneity (Section 5.6).

Section 5.5 elaborates on several layers of heterogeneity. Section 5.5.1 shows that the information embedded is heterogeneous. Section 5.5.2 reveals that the component signs of mechanism diagrams are also heterogeneous. Section 5.5.3 discusses an inter-referencing pattern of uniting diagrams and data images. Such a pattern is beyond merely displaying two kinds of visuals in parallel. It makes a new context of the whole, where the component visuals gain novel signifying functions and epistemic roles. Section 5.5.4 maintains that some mechanism diagrams have supra-perspectives, which are narrating perspectives that represent the author's manipulation of perspectives within the cell models.

Section 5.6 argues that mechanism diagrams generate novel meanings because they are synthetic. Section 5.6.1 introduces a cartographic notion of "supersign" to support my argument on the power of mechanism diagrams in biological practice. This is followed by Section 5.6.2 and 5.6.3 which respectively elaborate the power of diagrams to assert ideas and engage users. Section 5.6.4 suggests that biological mechanism diagrams are constantly in the state of becoming. They are fluid because they are part of the perpetual practice of constructing and defining models. This point comes from comparing the making of them with the making of maps.

Chapter Six concludes this study by re-addressing the three key features of diagrams: synthesis, heterogeneous, and engagement. Biological diagrams synthesise heterogeneous perspectives and are powerful to engage the user in two senses: in the dialogues amongst localities and with real-world intervention. I will then suggest potential topics for future research within this intellectual framework.

## Chapter Two: Literature Review

### 2.0 Preview

This chapter extracts the crucial ideas from the existing scholarship on visual representation, focusing upon their key connections to the analytical framework of this study. The research areas of these authors span from history and philosophy of science to art history.

This chapter chooses Daston and Galison (2007) to be the start, for it has good connections to the other sources. There are also intricate connections amongst the other authors' key concepts. Section 2.7 provides an overview of their connections. Below is a brief preview of the key contributions of these sources.

Section 2.1 centres on three ideas about the role of images digested from Daston and Galison's history of objectivity in scientific representation. The ideas are: (1) images as material embodiments of different virtues of objectivity, (2) the shift of images since the late twentieth century from representations to presentations, and (3) images as tools for producing useful knowledge. These three ideas have linkages to most of the sources reviewed in this chapter. Section 2.2 will introduce three sources on visual languages: Rudwick (1976), Ferguson (1977), and Gooding (1990). The first two are pioneering works in the history of scientific visualisation, both arguing for the crucial roles of diagrams in developing theory in science or technology. Both sources attempt to counterbalance the once mainstream focus on literacy and numeracy in history of science and technology. While these two works are relatively early, their argument that imagery acts as the vehicle for ideas in some disciplines is still useful for emphasising the role of visualisation in scientific discourse. The latter, Gooding's philosophy of Faraday's drawings, echoes with these two early works.

Then Section 2.3 will introduce the notion of “knowledge mapping” from Rasmussen's case study (1997) of electron microscopy. Data from electron microscopy was accepted through scientists “calibrating” novel images against the existing knowledge established with light microscopy. Mapping of knowledge between novel and existing fields is comparable to mapping of knowledge between different domains of research that probe the same phenomena. The latter often happens in biological mechanism research.

Section 2.4 reviews two works on biological mechanisms: Bechtel (2006) and Craver and Darden (2013). Both focus on the characterisation of contemporary biological mechanism research. They contribute to this study with some key features of biological mechanism research, and this study will show that the diagrams reflect such research cultures. Firstly, mechanism research is meant to integrate multi-level and multi-layer components (such as information about entities, activities, and relationships) of mechanistic explanations for biological phenomena. Because the components are investigated in different fields, such integration is an inter-field convergence of diverse systems of practice. Secondly, diagrams are advantageous in conveying the complexity of such inter-field integration. However, both works tend to concentrate on the building of mechanistic models rather than representations of them, leaving the active role of diagrams in mechanism research unexplored.

Section 2.5 reviews three central notions of my framework drawn from Bender and Marrinan (2010) and Wood (1992, 2010). Bender and Marrinan's work is an art-history analysis embracing diagrams across a range of disciplines through a long historical period. It has even treated some non-visual forms of representation, such as theatre and statistics, as “diagrammatic knowledge”. The key message from the authors is that “diagrammatic knowledge”, whether in pictorial forms or not, always synthesises heterogeneous information and engages the viewer in the process of new



meaning generation. The three notions extracted from this argument—heterogeneity, synthesis, and engagement—constitute the scaffold of my analytical view for biological diagrams. Wood's cartographic study resonates with Bender and Marrinan in terms of these three notions. He elaborates the notion of "supersign", which this study will use to characterise biological mechanism diagrams (Section 5.6). A supersign can be briefly defined as a synthesis of heterogeneous signs. The relationships between the component signs give rise to the meaning of the supersign as a whole. The meaning does not exist when the component signs are present alone and separately.

Section 2.6 will get back to my focus on biological diagrams per se by reviewing Lynch's study (1990, 2014) of making diagrams through transforming photographs. Lynch argues against the simplified view that diagrams are merely schematic versions of photographs. His case study shows that expert judgement plays an active role in the making of diagrams as "transformative renderings" from photographs. Lynch also discusses visual elements that are not transformed from photographs and represent relatively abstract ideas. But according to the results of this study, this feature of biological diagrams had not been really obvious until the rapid growth of mechanism research in recent decades. Therefore, this section will show how Lynch's study serves as a start for a richer discussion that captures the complexity of biological diagrams in the era of mechanism research, which Lynch's study has been too early to witness.

Interestingly, as historians and philosophers of science have focused on formal and linguistic forms of scientific discourse, studies on visual representation have been growing faster in the recent two decades. Since late 1980s, sources on visual culture have become increasingly abundant. Thus this study had to omit a considerable number of works that do not directly contribute to the analysis. Sociological studies of visualisation are excluded, despite that they provide important analyses of scientific practice<sup>16</sup>. Philosophical analyses of visual culture in art and science (especially their interface) are not considered<sup>17</sup>. Although this study will superficially mention some semiotic implications of biological diagrams, semiotics-driven studies of signs are not especially useful to this study<sup>18</sup>. Cultural studies of visualisation are also excluded, although two points reiterated by cultural studies are noteworthy: (1) contemporary society has entered an era of visual culture, (2) new visibility (eg. on the mass media, or in art creations) is emerging<sup>19</sup>. However, this study will explore the idea that visualisation in science does not necessarily become more complex merely due to new technologies. Finally, sources specifically concern the impact of digital technologies on the practice of image-making are not chosen, though recent growth of the field tends to reflect on the relation between scientific visualisation and technology<sup>20</sup>.

## 2.1 Useful representations: Daston and Galison (2007)

This section introduces three points that connect Daston and Galison's argument on the historical concepts of objectivity in scientific representations to my analytical framework: the plurality of ideas about "right depiction", images as presentations, and utility of images<sup>21</sup>.

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<sup>16</sup> Two examples are Pinch (1985) and Amann and Knorr Cetina (1988).

<sup>17</sup> For example, see Frigg, Roman, and Matthew Hunter (2010).

<sup>18</sup> For example, see Goodman (1976).

<sup>19</sup> For the relationship between science and society in terms of visual culture, see Huppauf and Weingart (2007). For visual culture of this century, see Bentkowska-Kafel et al. (2009); Grau and Veigl (2011).

<sup>20</sup> With regard to digital visual culture, a point should also be noted here. This chapter reviews two articles on representations by Lynch in 1990 and 2014. The 1990 work specialises biological diagrams, and the 2014 work seems a "rethinking" version in the digital era (Lynch, 2014). However, this study is not concentrating on the relationship between digital technologies and scientific representation, which belongs to the scope of the volume. Lynch's 2014 work is introduced in this study as an extension of his 1990 work.

<sup>21</sup> I am mainly concerned with images as presentations (see my definitions of "presentational supersigns" in Section

### 2.1.1 Right depiction: plural virtues and new spirit

The first connection comes from the authors' arguments that different virtues of objective representation have emerged in different times and that the plurality of these historical virtues is retained in scientific practice of representation. What counts as “right depiction” in scientific practice has never stood still. The authors reiterate that, while the paradigms of objective representation remained shifting, later paradigms did not replace earlier ones but digested them into the new pursuits of objectivity. Trained judgement emerging in the twentieth century did not replace mechanical objectivity of the nineteenth century, and both trained judgement and mechanical objectivity are still somehow embodied in a novel kind of “images-as-tools” emergent in the late twentieth century. This study does not deal with the problem of objectivity but focuses on how contemporary biological diagrams can be studied by borrowing Daston and Galison's “right depiction”. That is, what value is pursued by contemporary biology and embodied in the diagrams?

Biological diagrams surveyed in this study are very different from Daston and Galison's cases, which are atlases and data images. But the authors' pluralist view for objectivity is useful for analysing the spirit of contemporary biology embedded in diagrams, which are images as novel as Daston and Galison's late-twentieth-century cases but not yet explored in their work. These diagrams are visual models used in biological mechanism research, and the making of their components obviously involves aesthetic considerations (see Section 2.3 for the difference between photographs and diagrams, Section 2.6 for literature that studies the transformation relationship between data and diagrams, and Chapter Four for the subjective features of diagrams). The iconographic resources composing such diagrams, though conveying knowledge assumed to be unbiased, are deliberately designed with aesthetic value. However, the coexistence of aesthetic value, subjective interpretation and unbiased knowledge in biological diagrams does not undermine their value. On the contrary, such a coexistence contributes to the effective conveyance of ideas in specialist communication. Chapter Five will explore how heavily the effectiveness of communication of biological diagrams relies upon aesthetics.

Just like scientific atlases produced through trained judgement in early twentieth century still included the virtue of nineteenth-century mechanical objectivity, contemporary biological diagrams embody the influences of previous pursuits of objectivity. The diagrams surveyed in this study are influenced by both mechanical objectivity and trained judgement. In biological practice nowadays, the ideal of mechanical objectivity still works to reduce the agency by human subjectivity from the process of data registration, though the practitioners have recognised human subjectivity as unavoidable and acceptable. In other words, while the source of data still works toward (but does not fully achieve) mechanical objectivity, the practitioners are already open to subjective interpretation and representation of the data. Taking Figure 2.3 as an example, both the existence and the functions of the cell components are translated from laboratory data, while they are represented by visual elements produced through the authors' subjectivity.

At the same time, expert judgement and interpretation made by scientists (and artists) based on their professional experiences serve another critical part of the making of biological diagrams. As suggested (but not elaborated) by Lynch (1990. See Section 2.6 of this thesis), professional interpretation is required for both reading and producing biological diagrams. Such “subjective” interpretation—where individual subjectivity plays a key role that machines cannot replace—functions

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2.5.2 and Section 5.6) and with the uses of diagrams as “working objects” (Section 2.5.1). The authors' arguments on scientific morals and the scientific self exceed the scope of this thesis. These two themes are central to their volume and influential in several disciplines, as highlighted in several reviews of Daston and Galison's book. See, for example, Goliński (2008); Jardine (2012); Pickstone (2009).

in all these processes: extracting and abstracting important information from photographs (data) that contain an overwhelmingly large quantity of details, visually highlighting the important information against the unimportant background, and thereby directing the viewer's attention to the salient part of information. Therefore, the diagrams produced in this way are *useful* depictions for communicative purposes, especially in the context of collaborative research. This feature certainly is influenced by the virtue of trained judgement, which has taken a very similar role in scientific atlas-making, as argued by Daston and Galison:

Interpolating, highlighting, abstraction – all were subtle interventions needed to elicit meaning from the object or process, and to convey that meaning – to teach expertise – through the representation. (2007, 348)

Trained judgement is an “empirical art” (2007, 331), and the expertise of it must be gained through practising how to read in the way the images inform. In modern sciences, such training of practice is normally systematic and education-based. The professionals (including scientists and artists) equipped with trained expertise are self-confident in interpreting what is important and what is not in the images. Daston and Galison summarise four features of trained judgement: it recognises similarity relations that help build up criteria for patterns; it is intuitive and thus might either be conscious or unconscious; it is holistic because it pays attention to the general appearance more than restricting the vision to quantitative details; and it cannot be done with merely mechanical measures. Nowadays these features are still present in biological images (including both data and diagrams).

While the above traditional virtues (mechanical objectivity and trained judgement) are still seen in contemporary practice of making biological images, I suggest that biological diagrams embody a novel spirit of practice. This spirit concerns the interaction between different practices to avoid the limitation of a single point of view for biological mechanisms and that diagrams embody this pursuit because of their mediating role in the communication amongst local interests. This study considers diagrams as a visual form of communication and conception, following the theses of both Rudwick and Ferguson (Section 2.2). Effective communication (both visual and verbal) is required for the research community to collaboratively share knowledge produced by different contexts, especially in the era of mechanism research that always involves interaction amongst diverse fields of practice (see Section 2.4). In such a context of practice, the judgement is made through integration of, and sometimes competition between, diverse perspectives for the same biological phenomena. No single point of view is able to dominate the collaboration for modelling. I will get back to this point in Section 5.5 and Section 5.6, where I argue that the diagrams synthesise heterogeneity.

Thus it can be said that mechanism biologists in the period surveyed in this thesis work toward interactions amongst multiple perspectives, upon which they make the judgement that is not dominated by any single point of view. I imported the notion “perspective” from Bender and Marrinan’s thesis (2010), where it refers to different means of understanding the world (especially because their case study spans a range of disciplines). In Section 2.5.1, I will introduce Bender and Marrinan’s use of this term, which is different from the traditional art history use in the discussion about the actual angle of observing and painting. Briefly, my use of perspective is close to Bender and Marrinan’s notion. It refers to the local point of view for the subject matter and can embed aims, theories, methods, explanatory frameworks, values and so forth. The pursuit of interaction (which normally include integration and competition) amongst multiple perspectives emphasises contributions from a range of practices, as practices in contemporary biology have been differentiating into various areas of interest and are equipped with very different tools. In this sense, biological diagrams act as the media for competition and integration, helping the community obtain judgements and develop inquiry shared by different research interests.

Now that my use of Daston and Galison's pluralist view for “right depiction” has been introduced, certain links between their thesis and the other authors reviewed by this chapter appear more clearly. With regard to training and visual culture in science, both Rudwick (1976) and Ferguson (1977) who specialise in two different visual-oriented disciplines argue for the importance of practice in the visual traditions of their disciplines. Section 2.2 shall introduce these two authors and their emphasis upon visual tradition. Besides, their theses have more implications in terms of the role of visual representation in science and technology. Daston and Galison's thesis studies scientific visibility in a generic sense, while both Rudwick's and Ferguson's specialised accounts show that imagery in some disciplines requires individual interpretation and expert judgement to a greater extent<sup>22</sup>. This is because, for these disciplines, visual representation is the pivotal means of communicating and thinking. On the other hand, Section 2.6 will introduce Lynch's view for the actions taken by diagram-makers in biology to make transformations, as well as my suggestions for extending his view. Both require trained judgement for the making of useful diagrams for research purposes. Along with the important role of individual interpretation, Daston and Galison points out that the viewing process in the ethos of trained judgement “demands more from its recipient” (2007, 360) than it used to in the ethos of mechanical objectivity. The viewer of the scientific atlas had once been a passive “spectator”, whereas the viewer since the emergence of trained judgement actively participates in making the representations meaningful. This notion of active reading nicely echoes with how Bender and Marrinan characterise the interpretation of diagram meanings (2010, see Section 2.5.1<sup>23</sup>). Bender and Marrinan share the fundamental idea with Daston and Galison on the viewer's active reading, while going further to discuss the generation (ie. more than interpreting) of meaning of diagrams and treating this active reading as the *engagement* of the viewer.

### 2.1.2 Presentation

The second connection between Daston and Galison's arguments and this thesis concerns the shift of imagery from representation toward presentation since the second half of the twentieth century. This shift is implied in the aforementioned interpretation required from the active reader:

Explicitly “theoretical”, the new depictions not only invited interpretation once they were in place but also built interpretation into the very fabric of the image – but they did so as an epistemic matter. Theirs were exaggeration meant to teach, to communicate, to summarize knowledge, for only through exaggeration (advocates of the interpreted image argued) could the salient be extracted from the otherwise obscuring “naturalized” representation. The extremism of iconography generated by expert judgement exists not to display the ideal world behind the real one but to allow the initiate to learn how to see and to know. (2007, 360)

Namely, the images made with trained judgement now embed an attempt to develop and assert theory. Since the late twentieth century, this attempt acts more promptly and thus makes visual representations in various sciences no longer “re-presentations” of existing knowledge but presentations of novel and original ideas. In biological diagrams, sometimes this attempt seems less obvious, when the images aim to resemble what is observed, eg. biological objects. Sometimes this attempt is obvious, when the images aim to illustrate models, eg. hypothetical mechanisms.

22 Both authors' works on visual representation were very pioneering (in 1970s) and surely earlier than the launch of Daston and Galison's terminology, eg. trained judgement. But Daston and Galison's concepts are comparable to these two authors, especially when Rudwick discusses the role of geologists' subjectivity in making theoretical diagrams, and when Ferguson discussed the mental process of technologists during design-drawing.

23 Bender and Marrinan cite several works of Daston and Galison with respect to “working object”. But in terms of treating active reading as the viewer's engagement, there seems to be no explicit link made in their argument. This study notices their connection and explicitly points it out.

Previously, in the emerging period of trained judgement, scientific visualisations were mainly about atlas-making, and the atlas-makers (again including scientists and artists) still tended to re-present theories they extracted from observation of nature. Since the late twentieth century, images increasingly served scientific research with much novelty during the process of theoretical development. This is partly because of (1) the rising culture of simulation, where computer diagrams of things are the facts themselves and partly due to (2) the emergent interventionist view for scientific research, where images are the tools for scientists to make use of knowledge. In this new context of image production, the previously-subtle role of images as presentations becomes increasingly discernible. Images are no longer necessarily produced after the facts but are facts themselves. This feature is distinct from traditional atlases that copied what was already known to provide evidence of nature. In the authors' term, images are traditionally evidence and nowadays tools. They are tools in the ways they are employed to both produce knowledge and intervene in the use of knowledge. The latter will be reviewed in the following subsection. These two positions of "images-as-tools" actually are intertwined in the new science-engineering ethos of contemporary sciences, including biology.

The authors drop the prefix "re-" from "representation" to characterise "new images" (in the age of manipulating images as part of knowledge production process). Yet I should add that introducing the term "presentation" to characterise these new images suggests a deeper meaning corresponding to the other authors reviewed in this chapter. Daston and Galison term the new images "presentations" because:

- (1) The role of images becomes interactive, "no longer necessarily focused on copying what already exists – and instead becomes part of a coming-into-existence" (2007, 383).
- (2) Images nowadays can be displayed in an entrepreneurial sense, serving to persuade and promote.
- (3) The new images in various sciences (such as the authors' examples from nanotechnology and human science) are no longer "competing with art or even employing art but positioned as art itself" (384).

While the second characteristic mentioned by Daston and Galison is not related to this study, the first and the third sensibly describe biological diagrams. The first point is about originality and novelty of ideas conveyed in the visuals, and the third point is about the disappearance of science-art dichotomy because a number of scientific diagrams (which still function as working objects) are now produced with deliberately-artistic design.

The first characteristic is comparable to Rudwick's two-decade-earlier work on geological diagrams (Section 2.2), as Rudwick's historical account for the development of geological diagrams argues for the "formalisation" of images. Formalisation in Rudwick's use refers to the process that the concepts conveyed by geological diagrams in the early nineteenth century increasingly shifted from observations of tangible objects to more theoretical and abstract ideas, such as causal explanations and extrapolations. In other words, geological diagrams at that time gradually tended to visualise ideas that are not repeating what already existed. This tendency parallels the novelty and originality of ideas materialised by the new images in Daston and Galison's thesis, though concerning quite different forms of art. Both cases act to assert ideas (through manipulating images) that are assumed to be original in the field. Section 5.6 will discuss the assertive power of diagrams and show that certain biological diagrams can be situated in the intersection between these two sources. This situation especially unfolds when diagrams of the mechanism type (see Chapter Three for my taxonomy) display mechanistic explanations for biological phenomena. They implicitly attempt to persuade the viewer, as in Daston and Galison's sense.

The third characteristic about art-science fusion is the other matching point between Daston and

Galison's new images and biological diagrams. This study uses the term "fusion" to imply simultaneously (1) the previous distinction and competition between science and art and (2) the recent trend of scientific images being produced as artworks in many instances. While Daston and Galison focus on depictions of objects (such as simulated nanotubes and human anatomy), they have touched some depictions of phenomena in the case of fluid dynamics. For the scope of this study, the case of fluid dynamics is still too scientific data-oriented and less art-driven. Although given the "deliberate aestheticization" (2007, 402) of simulation images (such as colouration), scientific images in their examples largely remain in the category of data. Counterpart examples in biology are data graphs. This study concerns only diagrams but not data images. The results will show that diagrams, while having the forms of artworks, are also capable of presenting original ideas. This is how they embody the art-science fusion. Some diagrams surveyed in this study function like Daston and Galison's case of human anatomy image gallery. Such images are less like data but are artistic transformations of ideas about biological objects. Meanwhile, some other diagrams appear as true art, yet are capable of conveying highly complex ideas (such as mechanistic explanations). They are made as art that has much freedom in employing styles and visual elements beyond what is only available through scientific means (for the most interesting cases, see Section 5.3).

Such "art" exhibits a great degree of transforming abstract knowledge to iconography. As Chapter Four will show, it is not even odd to use purely decorative elements without much scientific sense in technical communication. Intriguingly, these alternative "artworks" are in many cases termed by the researchers "hypothetical models", "proposed mechanisms", or other names that do not point out their artistic features, as if they figure as *the* mechanistic models. This is to say that researchers transform their original ideas to a materialised form and that the form (no matter how "artistic" it is) itself is a display and a presentation of the ideas. In this sense, biological diagrams surveyed in this study exemplify and extend Daston and Galison's view for both presentation and art-science fusion.

### 2.1.3 Utility

Imagery plays a significant role in utility-driven scientific research in the age of science-engineering ethos. This is the third connection between Daston and Galison's thesis and my framework. In such an ethos, production and use of knowledge no longer have a hierarchical relationship but must take place at the same time, for the engineering-oriented inquiry concerns *workable* knowledge. Daston and Galison refer to Ian Hacking's interventionist view, which certainly is influenced by Bacon, that "*only use* (italics in original) could provide a robust realism":

It was a strong salvo in a long-standing debate over whether and under what conditions scientific objects may be taken as real. On the side of representation: we should take as real that which offers the best explanations. On the side of intervention: we should accept as real that which is efficacious. (2007, 392)

This study does not analyse biological diagrams in the aspect of realism but considers the growing emphasis upon utility of knowledge, as well as the impact of engineering-oriented thinking on the researchers' attitude to knowledge production. This section wants to maintain that, while biology does not appear as one of Daston and Galison's examples of manipulating images-as-tools for intervening in the world, contemporary biology indeed possesses utility-driven and engineering-oriented thinking in a different way. This is because biology since circa the middle twentieth century has shifted its view point from morphological, descriptive accounts to mechanical, explanatory ones (see Chapter One and Section 2.4).

Contemporary biologists in many sub-fields do not literally collaborate with engineers, they instead

*think of* explaining the phenomena in a mechanistic manner. As a result, they draw in a mechanistic manner when diagrams are required for both conceptualisation and communication of the explanations, just like that diagrams are the essential media in the engineering tradition (see Section 2.2.2 for Ferguson's argument on visual thinking in technology). Daston and Galison have raised examples from several sciences that are increasingly engineering-oriented, but they leave biology (although having mentioned in the text) as an arena that seems only remotely connected with the engineering tradition. This is true, but only in the sense that biology had not collaborated with engineering until the recent emergence of bioengineering-related areas. Regarding the manner of thinking, however, biological sciences have been thinking in a mechanistic way and producing knowledge in light of pragmatic value for decades.

Craver and Darden's account for pragmatism in mechanism research (Section 2.4) points out this aspect of biological sciences, in a way somehow complementary to Daston and Galison's discussion of the new science-engineering ethos in late-twentieth-century sciences. Also following Bacon, Craver and Darden's view for biological research suggests the intertwined and interdependent relationships between production and use of knowledge: knowing a mechanism enables one to change it or direct it to do desired work. This interventionist view for the role of biological knowledge in the world is very mechanism-specific, and mechanism is how nature phenomena are mostly studied in contemporary biomedicine. This mechanistic, pragmatic manner of treating knowledge is at the same time the motivation for inter-field convergence, wherein images play a crucial role as the media for inter-field mapping of knowledge (see Section 2.3).

Daston and Galison do not mention diagrams in biological research while discussing “images-as-tools” in this science-engineering ethos, leaving biological diagrams—as in the mechanism-oriented and utility-driven context—an unexplored terrain. Daston and Galison divide new images since the late twentieth century into “virtual images” and “haptic images” according to their different degrees of involvement in modifying the physical world. Virtual images are normally stored in digital archives, depicting real-world objects and subject to artistic modification by individual users. The author's example of interactive images of human anatomy is of this kind, which acts as “presentation” because every user is allowed to create one's own and novel versions that no one else has produced before. Haptic images, on the other hand, take a more active role in scientists' intervention in the physical world. The authors' example of nanotubes simulation diagrams is of this kind. This kind acts as “presentation” not only because it does not repeat what already exists but also, more importantly, because it displays ideas to persuade and entice the viewer. This kind figures more constitutively in knowledge-production in the new science-engineering ethos of research, as “ontology is not of much interest to engineers”, who focus on “what will work” (393). The virtual kind mainly functions to virtually present objects, whereas the haptic kind shows how to intervene in the behaviour of objects.

This study will reveal that diagrams in biological mechanism research form a different family in addition to the virtual and haptic kinds. They also exhibit the novel features of both kinds, spanning from presentation of ontology to map for intervention. Here, two prevalent types of diagrams found by this study are relevant. “Presentation of ontology” that parallels Daston and Galison's “virtual images” refers to what this study calls the “object type” of diagrams; “map for intervention” that parallels “haptic images” refers to the “mechanism type” in this study<sup>24</sup>. As this study will explore, the majority of “object diagrams” in biological mechanism research are about structural information of molecules at different levels. These images are definitely virtual, for they use various manipulable formats to represent the existence of objects. On the other hand, the typical appearance of “mechanism diagrams” is shown in Figure 2.3 and 2.4. Images of this kind illustrate the component entities and component activities in mechanistic models for particular phenomena. While they can be considered as paralleling Daston and Galison's haptic images, they are visually

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24 See Chapter Three for definitions and Chapter Four for the contents of these two types.

very different from those physics cases, and they certainly are not materially related to the experiment like the physics cases are. Thus they are involved in the researchers' manipulation of real-world objects in a different way from the simulation images of nanotubes. This is why they are maps for intervention: while these mechanism diagrams are drawn from a similarly engineering-influenced, utility-driven standpoint, they require certain transformation of knowledge comparable to map-making (Section 2.5.2). Thereby they gain epistemic functions that mediate the real-world intervention. Section 5.6 will discuss such functions in detail.

## 2.2 Communicate and think with the visuals: Rudwick (1976), Ferguson (1977), Gooding (1990)

This section reviews three sources that explore the roles of visual language in three different disciplines: geological sciences, technology, and physics. These three sources reinforce each other by emphasising the importance of visual language in reasoning and communication.

### 2.2.1 Rudwick (1976)

Rudwick proposes to build an “intellectual tradition “which emphasises the importance of visual modes of communication in the history of science. As the focus of historians of science had not been shifted to visual objects until the late 1980s, this work is quite pioneering in pointing out the intellectual value of visual studies. Here I review four important points extracted from this landmark paper. The first two points serve as a social grounding for advocating scientific visualisation. The latter two points on the ad hoc history of geological visual language are especially relevant to the concern of this thesis. I shall introduce these four points and then elaborate on their connections to this thesis.

Firstly, as early as in 1976, Rudwick has recognised the lack of historians' attention to visual modes of scientific communication and asserted the communicative power of visual objects in scientific practice. Secondly, visual modes of communication should be treated as a language that is analogous to, and sometimes independent from, verbal language. Understanding a specialist visual language requires learning the rules and conventions agreed and shared by a particular community. The implication is that visual languages in this sense are like verbal languages that they compose part of the *identity* of a specialist community. This implication is supported by Rudwick's narratives on the parallel processes between the establishment of geologists' “self-consciousness” and the development of their widely-agreed visual conventions.

The third point is about Rudwick's ad hoc analysis of the formation of visual language in geological science. This formation involved a gradual and somewhat distributed integration of diverse traditions of (1) cognitive goals and (2) visual representation of the goals. In other words, the integration of previously-diverse visual languages into one coherent language is an essential part of the integration of intellectual interests and methods.

The final point is that the development of geological visual language had been toward the more abstract and theory-laden directions. The integration of different kinds of empirical, data-oriented images turned out to give birth to images that embedded more extrapolations and causal explanations. This argument implies that, I suggest, the geological diagrams had moved from representations of observations to presentations of hypotheses and theories<sup>25</sup>. Chapter Five will show

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25 While Rudwick explicitly treats the visual language in geological science as “theory-laden”, I consider the meaning of this term as somehow different from the theory-ladenness of representations argued by Hacking (1983). The



that such a trend has a comparative one in contemporary biological visibility.

Rudwick attributes the ignorance of visual language by historians of science to their mental processes, which have been set verbal and mathematical through their training in physics, ie. the most dominant discipline where historians of science were from at that time. The tradition of educational values emphasised literacy and numeracy, leaving visual thinking as an inferior aid to scientific discourse. Rudwick's focus on geological visual language is an attempt to counter this bias. His historical analysis shows that geological science is comparative to medicine and technology in the sense that these three areas all remarkably rely on visual communication.

I understand Rudwick's term "communication" as including not only the conveyance of ideas but also the storing of information and even the involvement in knowledge making. This can be told from his narratives. For example, as the mineralogical way of diagram-making was introduced to geological drawing for utilitarian purposes, the mining-driven enquiry was incorporated into the knowledge body of geological science. I suspect that Rudwick's phrase "visual modes of communication" in geological science actually concerns the visual vehicle for several aspects of practice in geological science. In this regard, the centrality of visual representations in geological science is comparative to medicine and technology, for the visual modes of communication are a reflection of visual thinking of modern geologists<sup>26</sup>.

Modern geologists are trained to interpret visual representations in a tacit way. Their reliance on visual communication implies the existence of an established framework of rules and conventions for the visual language. Rudwick's use of the term "language" suggests that the maps and diagrams in geological science have particular structures and elements, which are exclusively comprehensible to the members of the community. In other words, they are components of a specialist "grammar" for the visual language and have to be learned via professional training. Rudwick points out that the visual language of geological science had been developed toward an increasingly esoteric direction (Rudwick 1976, 178). That is, the understanding and use of such a language are limited to a trained circle. This development paralleled the fact that a special group newly differentiated at that time "came to call themselves 'geologists'" (1976, 178). This trained circle gained their identity through the establishment and acceptance of their own institutional rules, including visual conventions.

The visual conventions did not come from a homogeneous source. Instead, influences from multiple and diverse traditions can be traced, in terms of both the appearances and the goals of the visual representations. A good example of the convergence of heterogeneous traditions is the development of "geological traverse" and "geological maps" via the fusion of two drawing styles: (a) mineralogical sections, which served mining engineering, and (b) topological drawings, which came from the natural-history interest. Such contingent fusions of contrasted styles, be it utilitarian mining traverse or natural historical topographies, eventually gave birth to not only three-dimensional drawings of geological observations but also causal explanations for what have been observed (where the observations were to be conveyed to those who did not see with their own eye). During such contingent processes, experiments have occurred in terms of both style (eg. the colours used to represent different strata structures) and element (eg. the "key" to the meanings of different colours). Meanwhile, these visual trials not only registered observations but also translated verbal records to drawings. Such experiments led to the formation of new iconographic devices that (a) had own new meanings and (b) connected existing iconographic elements to new, emergent

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theory-ladenness of geological visual language is embodied when the geologists (1) intentionally make the images vehicles for theories and extrapolations and (2) consider the images (wholly or partly) as themselves theories and extrapolations. As Rudwick puts in his summary diagram of the history of geological visual language (1976, Figure 25), such "theoretical maps/ landscapes/ sections" embed a coexistence of observations and theories.

<sup>26</sup> Rudwick describes the gap of visual representations between modern geologists and their ancestors, where the expertise of their ancestors was quite diverse. Modern (since circa the early nineteenth century) geologists use visuals heavily to communicate, while both the quality and quantity of visuals before the modern time were poor.

cognitive goals.

I suggest two points to be derived from Rudwick's narratives of the convergence of drawing traditions. The first point is about visual experiments, which led to new iconographic devices, during the adoption and incorporation of one another by different traditions of representation. The second point is that the integration of different visual traditions had been intertwined with the integration of different ways of observing and enquiring. Both the newly-developed iconographic devices and the ways of integrating existing drawing traditions eventually became established frameworks for configuring and interpreting all information that these traditions brought to the new geological discipline. This thesis will show some resonant observations in biological sciences.

New styles and new iconographic devices enhanced the coding ability of visual elements of the drawings. More theoretical information was then imposed on the elements. The dimensionality of geological drawings became multiple—three-dimensional structures of the earth were combined with causal explanations and extrapolations, which added a time axis. The increased use of visual “codes” also required the user to learn newly-developed conventions and frameworks, so that the user was able to tacitly decipher the increasingly abstract visual language. The training of interpreting an esoteric visual language further led to the aforementioned establishment of social identity of geologists. I consider both the enhanced coding ability and the growing dimensionality as part of the shift (as Rudwick argues) toward “theoretical” and “formalised” drawings. This shift is also from pure observations to mixtures of observations and theories/hypotheses, from purely-empirical records to inclusion of extrapolations, from descriptive to explanatory accounts, and finally, from “re-presentations” of observed things (which are to be transmitted to others) to “presentations” of original theories (which do not repeat existing ideas).

Toward the end of his paper, Rudwick interestingly draws a diagram to summarise his history of geological visual language. As the diagram expresses multiple dimensions of those historical contingencies, it perfectly reflects the author's mindset of a visual communicator and visual thinker. Although visual thinking was once ignored by the mainstream of history of science, there are two exceptions raised by Rudwick. One is medicine, whose long and heavy reliance on images is very similar to biological disciplines, ie. the focus of this thesis. The other exception is technology, which would be insightfully explored by Ferguson, just in the year following Rudwick's paper.

### **2.2.2 Ferguson (1977)**

Ferguson argued for the importance of visual thinking in technology in a somewhat similar way to Rudwick's thesis on geological diagrams. The two authors resonate with each other in two senses. Firstly, they both urge historians and educators to pay attention to the visual modes of mental processes that dominate the practice in some disciplines. For Rudwick, it is geological science, and for Ferguson, it is technology (including engineering). Both authors, having published their works in quite close years (Rudwick: 1976; Ferguson: 1977), maintain an ignored yet important fact that, in scientific and technological practices, there are ideas that “cannot be reduced to unambiguous verbal descriptions” (Ferguson 1977, 827). Such ideas are best processed by visual means, such as drawings, and the practitioners (geologists and technologists) actually conceive their objects in pictorial formats. That is, the practitioners *think with* the images. For this sake, Ferguson argued for “visual thinking”, and Rudwick points out that the mental process of geologists are set to be visual.

Both authors find their ground for arguments in the history of visual communication development. Ferguson traced the “development of nonverbal thoughts” (827) dating back to the Renaissance, and he was worried about the outcome of abandoning visual training from formal education of apprentice technologists. While Rudwick need not worry about the preservation of visual training in

geology, he argues against the overwhelming emphasis upon literacy and numeracy in contemporary education systems of the history of science. In this regard, both authors are concerned about the marginalisation of visual thinking in formal education.

The second sense in which the two authors resonate with each other is that they both narrate the ad hoc history of visuality in their disciplines of interest. Ferguson's approach to the visual history of technology appears to be quite similar to Rudwick's approach to geological science, yet he had taken his argument further beyond Rudwick's "visual modes of communication". Ferguson stressed the notion of visual thinking. Namely, he argued more explicitly for the visual-oriented thought process that Rudwick suggests yet does not elaborate.

While both authors have detailed various historical contingencies that have contributed to the formation of visual traditions in their disciplines, Ferguson seemed to treat the tools and the techniques as equal impacts on the development of visual thinking. This is contrary to Rudwick's account for the history of geological visual language, where the practitioners' attitude might have been a more important factor than technological innovations (such as copper engraving). Ferguson considered the "inventions in graphic arts" (which included new printing technologies, pictorial perspective, and other pictorial techniques emerging in the Renaissance) as the key factors that "lent system and order to the materials of non-verbal thought" (830). For Ferguson, the new printing technologies have "vastly augmented" the quantity of spreading non-verbal information, and the new pictorial techniques led to the improvement in quality of non-verbal communication. The latter is described as "nearly as important as printing" (830), suggesting Ferguson's heavier emphasis on the importance of technological innovation than Rudwick's. On the other hand, Ferguson's account for the "quality change" resulting from pictorial techniques point out a feature of non-verbal communication and thinking. Namely, the "visual image in one mind could be conveyed to another mind" (830-831), and this was owed to the new drawing techniques. I consider such a feature as salient to inter-subjective interaction in any kind of communication, and that non-verbal communication relies upon rules and conventions as heavily as verbal communication. Those pictorial inventions and their later wide applications helped establish the conventions and grammar of the technological images, making it possible that the technological minds think within the same frameworks. Without such shared conventions and grammar, image-thinking would not have been introduced to the object-teaching scheme in elementary school. Although Ferguson did not spell out the importance of shared rules of visual thinking in his history of object-teaching, it is quite plausible that pedagogical utility of visual images could not have been recognised in schooling since the seventeenth century (832) without the capability of inducing common thoughts in different minds. Therefore, drawings in technology tradition are not only a kind of communication (like Rudwick's geological visuals) but also a means of simultaneously representing and provoking thoughts.

In Ferguson's account, technological drawings are more than representations of objects or working machinery, for they are in fact a part of the design process. This is because, when the technologists design their machines, the machinery is initially imagined in a more visual form (the form that the machinery will be physically built in) than a verbally descriptive form. As Ferguson argued, during the process of designing, the technologists virtually "see" the machine parts in the sizes and in action (828):

As the designer draws lines on paper, he translates a picture held in his mind into a drawing that will produce a similar picture in another mind and will eventually become a three-dimensional engine in metal. (828)

There is no need here to get down to the philosophical debates around "mental image", as Ferguson's point is that technologists think in a visual way. In such a culture of practice, the uniformed education through visual means is to ensure that all minds in the field reason about the

machines in a common manner. The technologists on the one hand are trained to think visually, and on the other do their design in an inherently visual way. The three-dimensionality of the machines and the dynamics of mechanical actions are difficult to convey with words alone, where visual means is easier to accommodate the multi-dimensional complexity.

Ferguson's historical narratives show that the non-verbal tradition in technology had already emerged naturally in the early practice, when the description text was merely complementary to the drawings. At that time, object-teaching had not yet been systematically introduced into formal education. In other words, although not trained in uniformed thinking styles, early machine designers already thought visually and communicated their concepts to peers through images. Ferguson's argument for non-verbal knowledge in education is based on the fact that the complexity of technological objects have long been and must still be understood through visual means. The problem-solving ability of technologists has long included and must still include visual reasoning.

### 2.2.3 Gooding (1990)

Echoing from the 1990s with the above two 1970s and historical authors of geology and of technology, Gooding's study of the making of images by nineteenth-century physicists (such as Faraday) provided a ground for situating visual studies in the integrated agenda of history and philosophy of science. I suggest two important points to be extracted from Gooding's thesis. They are complementary to the above authors by offering a philosophical perspective: (1) the centrality of visual reasoning in the practice of experimental science (while Gooding sometimes referred to the term "communication" when discussing the role of Faraday's diagrams, this term has a broader meaning that the scientist communicates with himself during the development of theories); (2) the interwoven processes of establishing a visual language and that both the representations and the observations are *made sense of*<sup>27</sup>. This thesis does not rely much on Gooding to develop the argument about visuality in biosciences because his work centred on the epistemology of experimentation, which is somewhat detached from my focus on visual representation.

The first point is about that the making of images is an activity of communication, both to the scientists themselves and to others. Visual representations of observations and experimental settings are, because of the insufficiency of purely verbal means, invented for communication in response to scientists' need to share the way of seeing phenomena. But more importantly, prior to public construal, the observations and the experimental settings must be consistently construed by individual scientists themselves through time. Gooding finely defined construal and elaborated its role in investigating and theorising phenomena:

Construals are a means of interpreting unfamiliar experience and communicating one's trial interpretations. Construals are practical, situational and often concrete. They belong to the pre-verbal context of ostensive practices. (1990, 22)

This "communicating-to-self" part of communication is thus prior to the communication in the "public" sense raised by Rudwick and Ferguson. The imagery serves firstly as an agency of stabilising the scientist's own and private experiential observations, and it secondly helps incorporate the observations into the collective memory of scientists in the social context. Just like Faraday had to put instructions for himself to read his previous drawings, the meanings of the images as a part of construal were ambiguous, for they are the visual records of novel observations. Such novelty makes not only the observations themselves but also the ways of seeing them *plastic*.

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<sup>27</sup> Gooding used the phrase "make sense of" to refer to various stages and aspects of experimentation, construal, representation, and so on. The two aspects I here cite the phrase for are included. The phrase is stressed to show how such "making sense" action is important in my understanding of his account.

To reduce this plasticity, the scientist communicates to his/her future self via the increasingly established ways of seeing. Eventually the scientist knows how to read the previous drawings in a conventional way. Note that Gooding used the term “read” to refer to Faraday's viewing and understanding of his own drawings in his lab book. This use shows the richness of meaning embedded in the images and is consistent with some authors I will review in the following sections. Once having gone through the scientist's self construal, the less-ambiguous and more-stable (Gooding 1990, 79) visual representations go to the wider community. It is through the repetition of such phases of communication that the initially-private experience of the scientist gains “the status of empirical knowledge” (80) in the social context.

The second point is about borrowing and using existing renderings (both visual and verbal) in the process of making the representations, where the meanings embedded are intelligible to others in the wide public. This is similar to Rudwick's and Ferguson's notions of development of visual conventions. Such a process is also about “making sense” of the observations and their representations in the construal, collectively but not privately. Neither Rudwick nor Ferguson has argued as extensively as Gooding about the translation of private experience to collective memory through visual convention, for the former two authors are concerned more about the history but not the epistemology in the formation of convention. Faraday's visual language (including both the elements and the concepts conveyed) developed toward a stable status and became communicable through at least two stages: (1) the invention of new ways of using existing renderings to represent novel phenomena, and (2) the statement of theory via using newly-established visual language. The borrowing of curves (ie. the visual aspect) and the importing of activity-describing terms (such as “concentration”, “convergence”) from geometrical methods belong to the former stage. Faraday also analogised the magnetic lines to latitude and longitude. The reading of representations normally relies on an available repertoire of experiences, so it is a good strategy to introduce new way of reading representations of novel phenomena via using established visual languages that already have particular meanings. I consider such borrowing and importing of existing visual renderings as making a correspondence between novel and conventional meanings. Such a correspondence is crucial to the emergence of meanings of the novel visuals.

The latter stage is when the more durable representations and their emergent meanings go into a “wider network of practices” (93). The meanings will still be altered and shaped according on the scientists' use, and in this network the meanings really “develop historically” (93):

Meanings emerged in an historical process in which an operational, descriptive vocabulary was integrated into larger networks of established practices, empirical regularities and theoretical concerns. (27)

Here I focus on visual representation. The development of the communicable imagery in the case of nineteenth century physics—from scientists' private notebook to public display—exemplifies Gooding's argument that the making of imagery is a social activity. It is ultimately social because one wants to not only “share a way of seeing the phenomenon” (71) but also, just like Ferguson suggested, share a way of thinking the phenomenon. Chapter Five will discuss that biological diagrams surveyed in this study are great examples of two important aspects of Gooding's thesis: (1) the role of visuals in construals (Section 5.5 and 5.6), and (2) the notion of developing new visual language through borrowing existing ones (Section 5.3.2).

## 2.3 Inter-field mapping and map analogy: Rasmussen (1997)

This section discusses the ideas of map and mapping from Rasmussen's (1997) history of electron microscopy. These ideas contribute to the analytical framework of this thesis and have a central

vocabulary: *map*. It must be clarified here that the use of this word in Rasmussen's argument refers to twofold meanings. Meanwhile, these two meanings are tied to each other, as explained below.

Firstly, the author elaborates on the *mapping* process between different fields in terms of knowledge and investigating practice. Such mapping leads to “fusion of horizons” (Rasmussen, 1997, 255) of diverse expertise and develops novel “scenes of inquiry”<sup>28</sup>. Secondly, the author also discusses some analogies between cartography and microscopic imagery<sup>29</sup>, where the images indeed function as maps for the researchers to orient, locate, and move themselves about in an unexplored terrain, ie. the inside of the cell. Another analogy between maps and microscopic images is that scale bars are required in both arenas. The scale bars act as standard references, against which images produced in different contexts can be related to each other, together forming a field of knowledge about the “terrain” of interest. I consider the use of standard references (where scale bar is just a kind of them) as crucial to the mapping. Mutual mapping between different fields of knowledge require certain shared standards so that the previously incompatible ideas can correspond within a common scene of inquiry, becoming able to fruitfully offer new directions of research.

In Rasmussen's history of electron microscope, such “mapping” mainly results from *calibration* of discoveries generated by novel technology and technique (ie. photographs taken under electron microscope) against accepted knowledge produced with established techniques (eg. photographing under light microscope). The new discoveries are mapped onto the known terrains of knowledge. Nonetheless, in this thesis, the key notion adopted from Rasmussen's “mapping” is not one-way calibration of any new practice against established ones but two or multiple directional calibrations of different fields of knowledge against one another. This thesis focuses on how inter-field practices of biological research (see Section 2.4) are embedded in visual representations but not the history of a specific practice. Therefore, Rasmussen's notion of calibration is adopted here to explain the process of inter-field convergence. The mapping of knowledge is a mutual process, where the reliability of knowledge generated in different fields is assessed when the interrelations amongst them are built so that they altogether contribute to the explanation for the phenomena (in this study, the explanations are in the form of mechanistic models). Thus this study does not concern the distinction between novel and traditional knowledge. In sum, inter-field convergence is considered in this study as a *mutual* version of what Rasmussen describes as calibration of novel techniques in experimental science:

The experimenter must make a novel device behave itself in the range of phenomena accessible to established techniques, and develop theory of the technique to assess its reliability in the new range of phenomena, but this operation requires reference to established techniques and theories that are open to reinterpretation in the light of new device and the novel phenomena it brings to light. (1997, 13)

This quoted concept in fact implies a potentially mutual process, in which the established theories are not entirely fixed but subject to reinterpretation in the newly-developed conceptual scheme. The new scheme is driven by the emergence of novel device and theory. At the same time, both the novel device and the novel knowledge must be assessed through means compatible with the established schemes. This study extends this idea to truly multi-directional processes. It maintains that Rasmussen's mapping, which is “important work because it coordinates and generates links between diverse fields of activity” (1997, 19), plays a significant role in contemporary research of biological mechanisms. The reason is exactly that connecting diverse fields of activity is important in biological research areas that concern complex mechanisms. For the sake of collaborative inquiry

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28 Rasmussen cites Nicolas Jardine's term in his discussion of set frameworks (both conceptual and material) for research in particular scientific paradigms, see 1997, 11.

29 In Rasmussen's book, the term “micrographs” are normally used to refer to the images taken under some kinds of microscope. Nonetheless, this term is not widely-adopted enough for clarity. To avoid confusion, I use “microscopic images” throughout this section to mean what Rasmussen refers to as micrographs.

of a particular phenomenon, diverse systems of practice that have different aims and epistemic activities<sup>30</sup> must be correlated through the mapping of their concepts onto one another. The result is a body of heterogeneous knowledge that is interpretable to its constituent fields. The mapping process requires a medium for exchange and sharing. This study will show that visual representations serve as important (though not the only) media, just like microscopic images (taken by both electron and light microscopes) have served as the collaborative media for calibrating novel knowledge in the early years of electron microscope.

Rasmussen introduces Patrick Heelan's application of hermeneutic circle to his study scientific experimentation<sup>31</sup>. He demonstrates how mapping between novel and traditional practices led to both the acceptance of a novel instrument and the fusion of knowledge between new and established fields. He splits the pre-understandings that the reader (who is the data interpreter in experimentation in the case of electron microscope) already has when encountering new data into three parts:

- ⤴ Vorsicht: figurative languages shared between the data and the interpreter (researcher);
- ⤴ Vorgriff: pre-conceptions about the data;
- ⤴ Vorhabe: practice required for interpreting the data.

The original notion of hermeneutic circle is about encountering, reading, and understanding of a novel text by the reader. Rasmussen does extend this notion to an analogy between text-reading in literature and data-interpretation in scientific experimentation. But I shall get back to this analogy later and mention its application to biological diagrams in this thesis. Here, I focus on the back-and-forth process of (1) calibrating new observations against traditional anticipations; and (2) mapping between novel findings and established knowledge. This is because of the importance of mapping knowledge in opening a “deeply conservative, self-fulfilling” (1997, 252) hermeneutic circle to potential interpretation and new expectation.

The opening of this circle is progressive, along with the subtle shift of established practice (Vorhabe) by new technology that produces new kinds of images. The shift occurs when “the users become embodied in it and improvise new practices especially for the new kind of picture they look forward to making” (252). Rasmussen's “embodiment” has a special meaning in his philosophy of electron microscopy. It refers to the conformity of the user to simultaneously the instrument and the practice required for using the instrument. Rasmussen describes in detail the private experience of the researcher using electron microscope, which is a long and bodily process resulting in intimacy between the instrument and the researcher. The researcher is conformed to the instrument when such a process gradually eliminates one's awareness of the intermediation by the instrument. Thereby, the “Vorgriff of the microscopist is changed, progressively displaced as he or she develops a novel Vorhabe with the new instrument and the new kind of pictures it produces” (252). In such a process, a new field of practice evolves and a new way of interpreting emerges due to the change of pre-conception. The researcher who is previously-accustomed to the established system calibrates the new practice according to whether or not the new data is interpretable with established knowledge (253). The circle becomes less conservative, when new knowledge produced by the innovation can be mapped onto the known terrain.

In the case of biological mechanism research, as maintained above, the notions of “mapping” and “hermeneutic circle” are not about adopting a novel instrument by an established field but more about mutually and selectively adopting alien knowledge between different systems of practice. Such adoption is similar to Chang's (2012) “co-optation”, referring to different systems of practice

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30 This use of “system of practice” is in the vein of Chang (2012) yet has a slightly narrower meaning. Section 2.4 will provide a more detailed introduction.

31 The original notion of hermeneutic circle was borrowed from Dewey. See 1997, 248-249.

employing elements from each other to achieve their own aims (see Section 2.4 for details about interaction amongst those systems). In such a case, each viewer of biological diagrams (especially mechanism diagrams) from different fields has one's own pre-understandings of the particular phenomena and own hermeneutic circle of data interpretation. It must be through mapping between these diverse pre-understandings that the interpretations from fields alien to each other can be used as the ground for collective inquiry of the phenomena. Therefore, in biological mechanism research, mapping between knowledge produced by heterogeneous practices prevents researchers working in different cultures from "studying different worlds" (152). In Rasmussen's view for the history of innovation, standardisation is the key to researchers' systematic treatment of experience of the world. In the case of mechanism research, nonetheless, it is less about standardisation of instruments (due to the necessary heterogeneity of practices) and more about having a certain reference of mapping, which facilitates systematic interpretation of data and ensures coherence of the research project.

The mapping process and the hermeneutic circle shifted by mapping have another layer of implication, where Rasmussen's "text-reading" analogy is applicable to this study of biological diagrams. The viewer of diagrams in biological mechanism research usually is at the same time the user, who approaches the diagrams with one's own pre-understandings about the iconographic components of the diagrams. That is, just like data-interpretation, image-interpretation in such a context also involves the three ingredients of hermeneutic circle:

- ⤴ Vorsicht: shared *visual* languages between the contexts of production and viewing;
- ⤴ Vorgriff: the viewer's pre-conception of what is visualised and conveyed by the diagrams;
- ⤴ Vorhabe: the viewer's skills required for interpreting meanings of the diagrams.

Chapter Four and Five will reiterate that the viewer of biological diagrams is turned into the reader, for the "viewing" is in fact about active interpretation rather than passive perception<sup>32</sup>. Rasmussen considers scientists as more like the author than the audience of a book. But here the useful point of applying hermeneutic circle to biological imagery is that the image is an "interactive medium" for dialogues between the reader and the represented ideas, exactly like Rasmussen treats the microscopic images (1997, 255). The dialogues may shift the viewer's hermeneutic circle *of visual thinking*, leading to a "mapping" of conventions between the components of the diagrams and the viewer's context. Furthermore, in the case of biological mechanism research, I extend the notion of interactive medium to treating images as the media for epistemic interactions amongst different fields of practice. The above-mentioned systematic and collective manner of inquiry must be obtained through mapping amongst heterogeneous knowledge, where the mapping invites epistemic interactions. Images play a significant role in mediating such interactions in specialist communication.

The second meaning of Rasmussen's use of the term "map" is tied to some analogies between microscopic images and maps, and between experimenters and cartographers, "in terms of representational conventions and of underlying intuitions in the visual understanding of space" (1997, 234). Rasmussen does not pursue "the implications for maps" (234), but this study will. This study picks up what is left by Rasmussen because it concentrates on a highly complex kind of imagery, ie. biological diagrams, which can be compared to maps in the sense that both are meaningful configurations of heterogeneous signs (see Section 2.5 and 5.6). Microscopic images do not exhibit such a feature, so it is not surprising that Rasmussen parallels microscopic images with maps from two other aspects. One aspect is that *kinaesthetic experience* (though this vocabulary is mine, not his) significantly figures in the visual understanding of space in both microscopic imaging and map-using. Map-using refers to the "bodily" experience of conceiving the space via following

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<sup>32</sup> This argument is grounded in these theses: Daston and Galison (2007), Bender and Marrinan (2010), and Wood (1992). The second two are reviewed in see Section 2.5 of this thesis.



the orientation depicted in the images (maps and microscopic photographs). The other aspect is that particular uniform standards, eg. scale bars, are required for relating not only different maps but also different microscopic images to others. This is about how both the map-user and the researcher ensure an object depicted in an image to be identical to another object depicted in another image. This is to say that uniform standards help counter the incommensurability between data produced by different practices. The latter aspect is especially useful to this study, not because this study borrows Rasmussen's entire notion of uniform standards in both cartography and microscopic imagery, but because the biological diagrams surveyed in this study simultaneously exemplify part of this notion and suggest an unexplored extension of it. Below I will introduce the former aspect, namely the role of kinaesthetic experience in image-reading. Then I will review both the contribution and the potential extension of Rasmussen' argument on establishing standards for cross-reference between images.

In Rasmussen's view, the experimenter is immersed in a virtual navigation of the microscopic world. Given the long and lonely hours devoted to "picture control", the experimenter is intimately connected to the instrument, where Rasmussen points out the personal and ownership-like emotion of the experimenter toward the microscope. The long hours are required to accomplish high quality of images, involving a number of manual operations and observations, and the isolation is necessary to avoid interference from the outside world. Such devotion gradually eliminates the boundary between the experimenter and one's instrument. The experimenter increasingly ignores the mediating techniques, as if they become transparent and, at the same time, an "organic extension" of one's sense organs and limbs (1997, 228). Thereby, the experimenter is "mentally positioning and moving" their body within an alien "territory" (237). Such an experience of visually understanding the space is very similar to map-reading, in which the user locates oneself within the symbolic elements via a nearly kinaesthetic approach:

Thus, the electron micrograph is read in a way that fundamentally resembles the way a map is read. And a map... is an abstract model of possible perceptions and actions, linked inextricably to the body's native spatial axes.... And beneath the level of explicit convention, in the realm of deeply ingrained pre-understandings, map users' and microscopists' understanding of space both depend on an implicit, usually moving body as a standpoint or reference point.... (238)

Using the "moving body as a reference point" during the navigation of the space results in a (quasi-)kinaesthetic experience of both the experimenter and the map-user, tightly tying the visual understanding of space to the illusion that one has physically been in the space. Rasmussen also mentions some elements that maps and microscopic images have in common, such as marks and letters. However, both the taxonomy and the meanings of such elements appear ambiguous and not elaborated in his discussion, perhaps because he does not intend to explore the implication of signs.

Nevertheless, Rasmussen considers that some signs imposed respectively to maps and microscopic images are necessary to making images produced by different practices *comparable* and *commensurable* to one another. These signs represent specific uniform standards used by map-users and microscopists to cross-reference between images they encounter in different contexts. Rasmussen maintains that both maps and microscopic images require certain common standards between different practices so that different images depicting the same objects are comparable to one another. He uses reference for scale as an example, as such elements appear in both maps and microscopic images. Reference for scale especially exemplifies his view for overcoming incommensurability in his case study, where electron microscopic photographs were adopted by existing practice that produces knowledge through light microscopy. To ensure that the objects captured by light and electron microscopes are the same things, researchers sought to "map" (in the sense of knowledge mapping, as reviewed in the first half of this section) between the visual information contained in these two kinds of data, which are obtained at very different degrees of

magnification yet under common standards of size. The reference for size, just like the scale bars addressed in map legends, is needed for the recognition of identical objects (or “landscapes”, in the language of electron microscopists) recorded in images produced at different scales.

This notion of countering incommensurability through establishing uniform standards shared by different practices opens up an intriguing aspect of biological diagrams for this thesis. Biological diagrams in mechanism research normally have no uniform elements or standardised reference shared by different communities. Such diagrams are not laboratory data but illustrations of ideas generated during biological mechanism research. Sometimes they depict experimental procedures, and sometimes the structures of objects. In some cases, such as cellular mechanism research, diagrams are more frequently about modelling the mechanistic explanations for biological phenomena. Thus such diagrams are special artworks conveying scientific messages at the interface between art and science, exhibiting a great degree of freedom in terms of both style and element. Yet scientists working on mechanism research from different perspectives recognise the identical objects represented by visually diverse signs and situated in models at different scales. The assumed incommensurability between the diagrams is, of course, partly compensated by some descriptive words as adjacent signs to the depictions. But different visual elements representing identical things are not always accompanied by descriptive words. Comparing Figure 2.4 and 2.5, how do scientists tell the same identity of nuclear factor  $\kappa$ B (NF $\kappa$ B) of (1) the three large signs in the middle of Figure 2.4 and (2) the ribbon pictures in Figure 2.5? These two groups of depictions do not have similar colours. Nor are they accompanied with enough words indicating their parts (except for “p50”). Their relationship is more about schematisation and transformation, which include reducing details and changing the appearance. In the taxonomy of this study (see Chapter Three), Figure 2.4 is a “mechanism type” of diagram, and Figure 2.5 is an “object type”. Such schematisation and transformation make way for using the data of the object (ie. the protein complex) in the visualisation of the mechanism. In other words, the scientific information about the structure of this protein complex is commensurable between Figure 2.4 and 2.5. While the information contained in the two groups of depictions are not entirely the same, the objects depicted are identical to each other.

In such an example (which is typical in contemporary biological visualisation), if there is anything serving as a standard shared by the different depictions of identical things in Figure 2.4 and 2.5, it should be the ideas about the protein complex (eg. the configuration of protein subunits). In this sense, the identity of the protein complex is comparable and commensurable between the different representations of it in different contexts. This is because the information embedded in the depictions is *stable* and thus transferable in its own right, despite the unstable ways of representation. This explanation refers to Morgan's discussion (Morgan, 2011) of scientific facts travelling in various forms and across different cultural settings. The facts are stable and can be used for new purposes in new contexts distinct from the cultures of their origin. However, the example raised in the comparison between Figure 2.4 and 2.5 suggests an interesting paradox in terms of “visual representation of fact”. While Morgan argues for the importance of words as companions to “imaged facts”, these two representations, as mentioned, have limited descriptive words in common. Also, Morgan's argument treats the material format of facts as the carrier vehicle and emphasises its role in facts-travelling, but the difference between the “vehicles for the facts” (about the protein) in Figure 2.4 and 2.5 is obviously not about material format. Both the representations are two-dimensional images subject to electronic storage and printing.

The difference between these two representations as vehicles lies in their relationships with the neighbouring visual elements. When the trained viewer encounters Figure 2.4, they recognise the shared identity by the depictions in Figure 2.4 and 2.5 upon noticing the role of the large signs in the pathway represented by arrows and words. The other way of telling the identity is through noticing that the signs in Figure 2.4 are a schematic version of Figure 2.5 (or other structural

diagrams like this) and have been transformed by artistic manipulation. Neither way has anything to do with companion descriptions or material format. The visual representations are versatile in terms of both appearance and meaning. Both the style and the meaning embedded (eg. the detail structure in Figure 2.5, or the symbolic existence in Figure 2.4) can vary by the context of use. Only the identity is stable, and some important part of the facts in one context may be taken for granted in the other context.

To get back to Rasmussen, such a case does not have a standard for depicting, and the trained viewer does not need a standard to cross-reference between Figure 2.4 and 2.5. This is because the common reference is not a visual element but a stable identity of the protein, despite that it is represented in non-standardised and versatile styles. These two groups of depictions of one protein simultaneously possess stability and versatility. Such a paradox seen in facts-travelling is yet to be explored by this study. Rasmussen's case study focuses on microscopic images, which are treated as data in science and definitely require standardised references. Morgan's thesis is more recent, yet the focus is on facts themselves generally discussed in a broad range of sciences. Section 5.3.2 and 5.3.3 will show that both the styles and the meanings of visual elements can be versatile and that the embedded concepts yet remain stable and transferable. Section 5.6 will discuss the possibility that some meanings of signs are kept stable through establishing relationships with other signs, regardless of their versatile use.

## 2.4 Biological mechanisms: Bechtel (2006); Craver and Darden (2013)

This section introduces the key features of biological practice of mechanism research extracted from the sources on biological mechanisms. The key features are important to my framework because the results of this study (Chapter Four) reveal a large—and still growing—emphasis upon mechanisms in biological communication since the 1990s. Along with the increase of mechanism diagrams in both relative proportion and frequency<sup>33</sup>, the contents of mechanism diagrams have evolved and proliferated. The complexity of mechanism diagrams stands out amongst all types of diagrams surveyed by this thesis. These intriguing results suggest that visual conveyance of mechanisms is plausibly a reflection of the features of mechanism research: what is so complex in biological mechanisms? It is thus relevant to bring the literature on biological mechanisms into this chapter.

Out of the abundant literature on mechanism<sup>34</sup>, I selected two sources on contemporary biology: Bechtel's history of cell biology (2006) and Craver and Darden's philosophy of biological mechanisms (2013). This selection is due to the focus of this study on biological mechanisms but not mechanisms in other sciences. Meanwhile, it must be clarified that, because this study concerns the visual representations used by scientists to represent (and perhaps also conceptualise) ideas about biological mechanisms, I shall concentrate on these authors' contributions to my discussion on the relationship between biological mechanism research and visual representation, instead of biological mechanisms per se. This section reviews these two sources in parallel and makes comparisons.

Three points extracted from these two sources together make crucial contributions to this study. The contributions are about (1) characterisation of biological mechanism research, and (2) the relationship between visual representation and biological mechanism research. These three points

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<sup>33</sup> These terms and their use in this thesis will be introduced in detail in Chapter Three.

<sup>34</sup> Illari and Williamson's paper (2012) proposes a generic characterisation of mechanism that aims to apply widely to different sciences. In the same paper they also review the main contributors to the debates around characterisation of a mechanism since Bechtel and Richardson's 1993 book: Glennan (2002); Machamer et al. (2000); Bechtel and Abrahamsen (2005).

can be connected to the other authors reviewed in this chapter. They together form the framework for my analysis.

Firstly, both sources argue on the integration of inter-level and inter-field perspectives in biological mechanism research, as biological mechanisms are meant to involve multi-level components that must be investigated by different fields of practice. This point has a quite clear connection to the multi-perspectivity of diagrammatic knowledge maintained by Bender and Marrinan (and Lynch, implicitly)<sup>35</sup>. As mentioned above, this study avoids the characterisation of mechanisms themselves but concentrates on the characterisation of the practice of biological mechanisms. Although the characteristics of the practice are surely tied to those of mechanisms, there is a distinction between understandings of the research object and of the research.

Secondly, diagrammatic representations have particular advantages in conveying the inter-level and inter-field features of biological mechanisms. For Bechtel, the advantages of diagrammatic representations are about both (a) simultaneous conveyance of multiple dimensions of the mechanisms and (b) representing complex ideas (such as the arrows representing blood flow in Figure 2.1). For Craver and Darden, the advantages of diagrams in representing biological mechanisms include effective conveying of multiple perspectives. They also discuss (a) the transformation of details of the real objects to relatively abstract representations, and (b) why such abstraction is important to the conveying of ideas that cannot be read from photographs. The latter concerning reduction of details and imposition of ideas has a link to Lynch's argument (1990) that diagram-making is not only simplifying but also deliberately transforming the pictorial elements to embed theories.

The third point specifically comes from Craver and Darden's argument on the pragmatic value of biological mechanism research. This study does not deal with the philosophical discussion about the nature of biological mechanisms but discusses the role of visual representations in the pragmatic value of mechanism research. Craver and Darden maintain that knowing how biological mechanisms work (ie. the causes of the mechanistic systems) helps the researcher develop devices for producing desired effects. Also in this pragmatic aspect, they argue that good theoretical schemas (compared to the rivals) for biological mechanisms are capable of simultaneously generating future inquiries and conserving established traditions (2013, 84). On the grounds of these pragmatic features of biological mechanism research, I suggest with the results of this study that diagrams play an important role in mediating the process of embodying these values in scientific practice. This is the connection between Craver and Darden's mechanism-oriented thesis and the art/semiotics-oriented theses of Bender and Marrinan and Wood (see Section 2.5). The embodiment of pragmatic value of biological mechanism research in some senses needs diagrams as mediators. This is because diagrammatic representations function to engage the user in the emergence of meanings. Such mediation contributes to the process where the new meanings offer a ground for the user to intervene in the mechanisms of interest. Thereby the knowledge of biological mechanisms does work in the world—borrowing Wood's language<sup>36</sup>—through the diagrams engaging the user in the interpretation and the use of ideas embedded in the diagrams.

The first point extracted from both sources concerns the integration of multiple and heterogeneous levels and fields in the mechanisms as wholes. Bechtel bases his argument on specialising the historical formation of cell biology discipline, and Craver and Darden discuss biological mechanisms in a generic sense. In both sources, understanding biological mechanisms requires identifying—from a “decomposing” point of view—the entities and activities that constitute the

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<sup>35</sup> For Bender and Marrinan, see Section 2.5; For Lynch, see Section 2.6.

<sup>36</sup> Wood maintains that maps have “discourse functions” that can influence behaviour via communication and are ways of “doing work” (2010, 2). This study treats biological mechanism diagrams as comparable visual constructs to maps. See Section 2.5.2 of this thesis for a review of Wood. Also see Wood (2010, 106-7) for his elaboration on maps’ discursive power.

mechanisms. Bechtel's mechanism can be decomposed into component “working parts” and component “operations” (55-59). Here I explain different authors' uses of special terms in characterising biological mechanisms. Bechtel's use of the term “operation” appears a bit ambiguous, but it actually can be paralleled to what Craver and Darden term “activities” and/or “relationships” in biological mechanisms. When referring to the two component parts of mechanisms, the terminology of this study is consistent with Craver and Darden (as well as Illari and Williamson 2012). This study terms the two kinds of component *entity* and *activity*.

Bechtel's history of formation of cell biology is about the inter-field interaction and collaboration between cytology (the science of structure) and biochemistry (the science of function). His historical narratives end with the institutionalisation of cell biology as a discipline. It is obvious that this novel discipline could not have been formed without the scientific inquiries being driven by the curiosity about possible integration of cell compartments (eg. cell organelles) and cellular functions. The cell compartments serve as the loci of the functions, and these two perspectives had been separately investigated. Bechtel argues that decomposition of cell mechanisms is divided into two: structural and functional decompositions, where the former recognises the locus, and the latter recognises the activity. Historically, the identification of cell structure and cell functions have been practised by cytology and biochemistry separately. But understanding how the cell works requires investigating the cell from a mechanistic viewpoint. Namely, the structure and the function must be mapped onto each other. Thus the history of cell biology is about scientists from these two disciplines acknowledging each other's potential contribution to the understanding of cell mechanism. It is also about scientists mapping the functions of cell parts on the cellular structures on an inter-level basis. Cell biology had become a research field before having been established as a discipline. The formation of this field is owed to inter-field and inter-level convergence. It is such a convergence that makes productive new tools available for integrative inquiries.

This integrative feature of biological mechanism research is argued by Craver and Darden as a nearly fundamental characteristic:

The science of biology must be integrated because it deals with a domain of heterogeneous phenomena, because mechanisms span multiple levels, and because mechanisms often operate at and across different time scales. (2013, 182)

This quote also shows the heterogeneity of knowledge to be incorporated into a whole. The authors certainly consider such heterogeneous knowledge as produced by diverse perspectives for the mechanisms, resonating with Bender and Marrinan's argument (and their treatment of Daston's thesis):

Often, however, biologists find it necessary to integrate what is known from the perspective of one field with what is known from the perspective of another. (2013, 161)

In other words, the component knowledge is heterogeneous because it is generated in different *systems of practice*<sup>37</sup>, which have different research concerns. For example, in Bechtel's history of cell biology, the cytologists cared about the structure, and the biochemists cared about the function.

With regard to the necessity of integration in biological mechanism research, the terminology “system of practice” used in this thesis should be briefly introduced here. This term will appear again in my discussion of synthesising different perspectives for biological phenomena (Section 2.5, 5.5, 5.6). Hasok Chang (2012) proposes this phrase to argue for pluralist historiography and replace monistic historiography (such as Kuhn's paradigm shift and Lakatos' competition of research programmes). The brief version of his characterisation of “system of practice” is:

By a “system of practice” I mean a coherent and interacting set of epistemic activities performed with a view to achieve certain aims. (2012, 260)

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<sup>37</sup> See Section 2.5 for heterogeneous systems of practice as heterogeneous perspectives.

Chang has detailed examples for “epistemic activity” (16), which spans across a range of actions scientists take to produce knowledge (such as predicting, modelling, measuring, etc.). The point is that, by emphasising the wide range of epistemic activities, Chang's view counters the traditional account of the history of science that tends to neglect the experimental and non-propositional, non-verbal aspects of science (15). In the case of biological sciences, the different research areas that have proliferated and integrated (and still are proliferating and integrating) certainly can be considered as different systems of practice, whose aims differ from one another. They have different sets of epistemic activities, including the way of representing the discoveries.

Chang's systems of practice in the same period are not isolated but interacting. Moreover, he elaborates on the scientific benefits of different systems of practice interacting with one another, where the historical picture has to be drawn in an actively pluralist view. This emphasis on interaction points out an important feature of biological mechanism research, serving as the connection between his notion and the sources reviewed in this section. In his argument on the benefits of interaction (ie. productivity resulting from (1) integration, (2) co-optation, and even (3) competition), Chang mentions Sandra Mitchell's view for integrative pluralism. Mitchell's thesis (2003) is based on the case study of biological complexity, such as evolution and social behaviour of insects, arguing against both isolation of levels (of complex systems) and a unification view for science. This is because the greatly complex characteristic of biological systems requires inter-level and inter-field interaction amongst different investigatory programmes. No united theory is possible to be made about the complexity in all situations. Hence the explanations must be plural. Mitchell does not explicitly argue about mechanism research but approaches biological complexity via using the term “models”. In the biological literature surveyed in this thesis, both terms are interchangeably used by practitioners. Thus her integrative pluralism is quite useful for reflecting the reality of practice in the field (she calls the condition that no integration is needed “ideal world”).

This study extends from these authors' theses on the integrative and interactive characteristics of practice. Section 5.5 and 5.6 will discuss both the integration embodied in biological visualisation and my idea about integration of perspectives by biological diagrams. Briefly, such visual integration does *not* really reduce the constituent perspectives but sometimes black-boxes them for operational reasons. By black-boxing I mean the reduced use of visual elements, where the informed viewer still recognises the contribution of particular perspectives to the whole mechanism. While sometimes the visual elements may be trimmed due to the limits of image sizes, both the information and the perspectives embedded in the diagrams are only black-boxed—and can be decoded by trained eye—but not sacrificed.

Both Bechtel and Craver and Darden discuss decomposition of biological mechanisms. This study links their discussion to the diversity of practices involved in developing a mechanistic model, viewing different components as resulting from the interests of different systems of practice. Craver and Darden's decomposition of biological mechanisms is similar to Bechtel's yet finer, including a range of “schemas” established from previous research. The schemas embrace entities (“working parts” for Bechtel), activities and relationships (similar to Bechtel's “operations”), and spaces and times. Craver and Darden assume the integration to happen across different sizes, spatial levels, activities, times, and time scales. Bechtel has a relatively simple description of such complexity of biological mechanisms. But he certainly recognises it, when he discusses the “orchestration” of spatio-temporal levels within mechanisms.

As this study is not concerned about mechanisms themselves but what is in mechanisms as reflected in their visual representations, I will not directly deal with the problem of whether or not biological mechanisms are to perform particular functions<sup>38</sup>. Thus Bechtel's emphasis on orchestration is not

38 See Bechtel and Abrahamsen (2005) for mechanisms performing functions, and Illari and Williamson (2012) for their suggestion of replacing “performing a function” with “responsible for a phenomenon”.

used, for it suggests a purposeful harmony amongst the components. Nonetheless, his notion of mechanism as a cohesive whole underpins my view for a feature of biological mechanisms that is profoundly reflected in visual representations. Despite his use of “function”, Bechtel's “cohesive system” explains the features of biological mechanisms reflected by diagrams surveyed in this study:

A mechanism is not just a collection of independent parts, each carrying out its operation in isolation. Rather, parts and operations are generally integrated into a cohesive, functioning system. (2006, 32-3)

Some authors are concerned about whether or not the term “system” is adequate to characterise mechanisms, for this term implies structured and stable features and does not have wide application (Illari and Williamson, 2012, 121). But again, such concern does not prevent me sometimes using “system” to characterise biological mechanisms in this study, as this study focuses on biological mechanisms *as represented* in diagrammatic models. Within the realm of diagrammatic representations, biological mechanisms are conceived as structured and stable because they are constructed for practical purpose. The diagram is a “single snapshot (or a series of snapshots)” that serves as an assembly of “all pertinent information” (Craver and Darden, 2013, 39). Therefore, the term “system” is adequate to characterise biological mechanisms as in their representations.

I quoted Bechtel above to maintain that (1) a cohesive whole is not merely a “blending” of the components and that (2) this cohesive whole can do something unachievable by the components being present separately. For example, it can “give rise to a phenomenon” (Craver and Darden, 2013, 65) that is to be explained with a mechanistic model. To summarise, the mechanistic model is a *synthesis* (this term, in Bender and Marrinan's vein, will be introduced in Section 2.5.1) of its component entities and component activities, generating emergent characteristics of the whole<sup>39</sup>. Then, bringing the aforementioned inter-field and inter-level integration to this notion of synthesis, models for biological mechanisms have a feature of synthesising heterogeneous perspectives<sup>40</sup>.

The second point extracted from these two works mainly concerns the advantageous features of representing biological mechanisms with diagrams. These two works resonate with each other in that diagrams use visual resources to convey complex ideas (especially the multi-level interrelationships within the mechanisms) and that diagrams are routinely employed in biological sciences to represent mechanisms. The latter describes how ideas of mechanisms are communicated in the actual practice. The former somewhat explains the latter—the complexity residing in mechanisms is challenging to purely verbal expression in terms of effective communication, where diagrams offer a solution. Although these two authors explore the details of these features of mechanism diagrams in slightly different directions, I shall include all of them in my “start-up kit” for analysing the complexity of mechanism diagrams. Craver and Darden's account for conveying the complexity by diagrams is derived from their argument that biological mechanisms are about multi-level integration. Diagrams have the capacity to embrace a range of components of the mechanistic story: entities, activities, relations, spatial and temporal orders, and so on. Of course, all these components are potentially multi-level and multi-layered. Bechtel's account for conveying complex components, similarly, emphasises the extensive use of two-dimensional space within the diagram image. Such use tends to employ arrows to represent the temporal dimension so that the two dimensions of the image are left free for representing information about space and relation. Such a strategic use of visual elements makes possible a simultaneous inspection of entities (working parts) and activities (operations). However, this simultaneous perception of components argued by both works may not be the most significant advantage of diagrams.

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<sup>39</sup> There is an abundant philosophical literature on emergent properties, which is beyond the scope of this thesis. I just borrow the term “emergent”, for it well-describes the novelty of the characteristics of the synthetic whole.

<sup>40</sup> Section 2.5 shall discuss related ideas in detail. Then, Chapter Four (results) and Five (discussion) will explain the reason for titling this thesis this way.

The significant advantage of diagrams in representing biological mechanisms, according to Bechtel, is their iconic feature (Bechtel's term) that cannot be substituted by text<sup>41</sup>. Figure 2.1 is an image Bechtel uses to demonstrate the “invaluable iconic resources for representation” (2006, 36). This diagram is a great example of mechanistic models for biological phenomena, as the pumping action of the heart is quite comparable to a true machinery. In this diagram, the viewer perceives the parallel yet opposite directions of the blood flows and at the same time conceptualises the scenario of blood flowing at different sites of the heart. The perception and conceptualisation occurring in the viewing process are both relatively direct compared to reading a text that contains the same information.

Here, I add two points as a preview of some results of this thesis. Firstly, upon viewing Figure 2.1, not only the parallel activities (blood flows at different sites) but also the possible existence of a causal relationship between heart-pumping and blood flow can be conceived by the viewer. The conception seems to be facilitated by a virtual animation of the pumping-to-flow process (similar to Bechtel's argument mentioned below). Thus the diagram has a deeper ability regarding explaining the represented activities, with exactly what is drawn in the image. The results of this thesis will show that the visual representations of more recent and more complex mechanistic models for biological phenomena (compared to Harvey's model of circulation) are increasingly capable of conveying explanations, apart from expressing descriptions (eg. the direction of blood flow, and the layout of heart chambers).

Secondly, the combination of heterogeneous components in diagrams gives rise to a richer kind of representation, which is more than the sum of its individual parts. Still using Figure 2.1 as an example, the blank space inside the visual representation of the heart can be understood as the inner space of the heart and the flowing blood (or more precisely, the heart chambers filled with flowing blood). But there is actually “nothing” drawn to realistically represent these concepts. It is the *relationship* between the blank space and the two visual representations that gives rise to the meaning of the blank space: the arrows (which must be understood as blood flow direction) and the words (which must be understood as the abbreviations for heart chambers and blood vessels). The emergence of the meaning of the blank space is somehow contingent: it depends upon the joint interpretations of the other visual representations next to this blank space. In Section 2.5, I shall review two sources on the importance of relationships amongst components within diagrams, and Section 5.6 will discuss how the relationships amongst the components of diagrams are critical for generating the meanings of the diagrams as wholes.

On the representational function of visual resources, the two works reviewed in this section have slightly different foci. Nevertheless, they both have suggested the importance of conventionality to the function of visual resources. Craver and Darden maintain that plural entities belonging to a special kind in biological mechanisms are usually represented by a single visual representation in the diagram. They treat such a conversion (of plural entities to a single visual representation) as the abstraction of details. Interestingly, this argument has an implicit connection to Lynch's argument (1990) about transforming details in observations to diagrams, where a family of entities is represented by a “model” diagram. In such modelling, the visual model of the entity does not resemble any specific single photograph in reality. The model is about figuring the typical pattern of the entity (see Section 2.6). Bechtel does not focus on the representations of entities. He on the other hand suggests the important role of arrows in pointing out the processes in biological mechanisms. This thesis will extend the discussion of arrows in Section 5.3.3.

Arrows in mechanism diagrams are mentioned by both works, but Craver and Darden only mention

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41 While both Bechtel and Craver and Darden use ‘icon’ and ‘iconic’ to refer to or describe some visual components of diagrams, they do not provide detailed definitions. Also, I understand their use of ‘icon’ as in a general sense that actually can include different kinds of semiotic signs. In Section 5.2, where I will start discussing the signifying functions of visual elements, I will define my use of different signs.



that arrows are normally used to represent abstract ideas, such as activities and relationships. Meanwhile, it is suggested in Bechtel's argument that arrows are key to compensating the limitation of diagrams in representing biological mechanisms. As diagrams are meant to be static and two-dimensional, they are inherently limited in terms of presenting dynamic features. This is compensated when the visual resources (eg. arrows) help the viewer simulate the continuity of processes and the dynamics of complex systems. Bechtel further refers to neuroscience study to argue that such imagery-supplemented “mental animation” of mechanistic processes is cognitively comparable to really seeing an animation of “a system in action” (2006, 38-39). He also points out the distinction between diagrammatic reasoning and propositional reasoning, implicitly (but intriguingly) resonating with Ferguson's argument for technologists' non-verbal thinking with diagrams (Section 2.2.2 of this thesis). Importantly, Bechtel has suggested a direction of querying how arrows (and other visual elements that help one mentally simulate dynamics) are key to visual reasoning of biological mechanisms. This direction involves studying the roles played by arrows in the visual syntax of diagrams. Chapter Four and Section 5.3.3 shall go in this direction with empirical results.

The third point of this section is specifically extracted from Craver and Darden's discussion of the pragmatic aspects of biological mechanism research. Before I bring up my main concern on the role of visual representations in the pragmatic context, I quote some passages that capture the spirit of the authors' argument on the pragmatic value of mechanism research. The authors consider that knowing a mechanism can help the researchers “devise new ways to control it” (2013, 186). Such consideration has a Baconian influence:

Bacon defined science as the search for causes and the production of effects. In this chapter we emphasize the relationship between these two aims. When one knows how a mechanism works, one can know how to work with mechanisms to produce new effects.... Perhaps not all knowledge is power, but mechanistic knowledge certainly is. And with this power comes new responsibilities: for the once intractable problems we solve, for the new problems we create, and for the now solvable problems we fail to address. (2013, 195)

Through introducing research cases at different levels of biological mechanisms, which span from ecology and organisms to cells, Craver and Darden demonstrate that pragmatic value of knowing a mechanism is embodied in controlling it and making desired effects. Such an argument is yet to be proven as universally true for biological mechanism research. The point here is that mechanism research engages the researchers not only when the researchers test and revise the mechanistic models but also when the models are used to make impacts on the world they live in.

The process of the former—test and revision of the mechanistic models—is also discussed by Craver and Darden, as they maintain two criteria for choosing a “good theory” amongst competing theories: fertility and conservation. Fertility is about providing “new avenues of research” and generating new research questions, and conservation is about retaining “crucial bits of what came before” and maintaining tradition against too dramatic breaking force (2013, 84). An open cycle of testing and revising the mechanistic models based on these two criteria leads to extension and expansion of the models. This is similar to Bechtel's description of the process of revising and substantiating the content of a growing mechanistic model (Bechtel, 2006, 61-62). In other words, the model should suggest new hypotheses and predictions, and the researchers are engaged in a productive cycle of testing and revising, so that new theories within the model will be continuously consolidated. Section 5.6.4 shall discuss the role of diagrams in contributing to the productivity of biological mechanism research from this pragmatic point of view.

## 2.5 Synthetic images: Bender and Marrinan (2010); Wood (1992; 2010)

This section reviews two works that analyse different kinds of synthetic images. Four ideas (as put in *Italics* here) are key to my interpretation of the biological diagrams analysed in this thesis: the *synthesis* of *heterogeneous* components of the diagrams takes place via building new *relationships* between the components and leads to *engagement* of the viewer. Bender and Marrinan, from the perspective of art history, study diagrams across a range of areas and times. Their notion of “diagrammatic knowledge” even touches non-image constructs, such as statistics and quantum mechanics. Unlike Bender and Marrinan's broad concern, Wood exclusively studies the culture and the history of maps. Although their scopes are different, they both have come to a conclusion about the synthetic characteristic of images of their interests.

Both works explicitly maintain (1) the heterogeneity of information embedded in the images they have analysed and that (2) these images should be treated as syntheses of diverse information. The uniting of diverse information and elements generates meanings that the components alone could not provide. Both diagrams and maps unite information<sup>42</sup> via building relationships between the components. Bender and Marrinan call this building of relationships “correlation”, and Wood claims that “maps are about relationships”. Given the complexity of relationships built in both diagrams and maps, both kinds of images require the viewer to be engaged with the process of meaning generation. Bender and Marrinan emphasise self-reflection of the viewer on diagrams. Wood emphasises the discourse function of maps. Namely, the cultural contexts of maps constitute a part of the power of maps to do work—through viewer engagement—in the world which they are produced.

### 2.5.1 Bender and Marrinan (2010)

Three arguments on the culture of diagrams are drawn from Bender and Marrinan, significantly composing the scaffold of my analytical framework for biological diagrams. The first argument is *heterogeneity* of components of diagrams. In Bender and Marrinan's language, this feature is the dissimilarity of information. Namely, diagrams contain dissimilar packets of data, and the ideas conveyed by diagrams are of heterogeneous origins. My framework extends this feature from information represented to the representational elements. The second argument is *synthesis*. Diagrams not only unite heterogeneous components but also produce new meanings of the whole. The meanings do not exist when the components are present alone. This argument derives from Bender and Marrinan's correlation, ie. diagrams correlate dissimilar things within the visual configurations and in a process-driven way. Here, I argue that the term “synthesis” is of special importance, for it suggests the capability of diagrams to produce meanings through building relationships between the components<sup>43</sup>. The third argument is *engagement*. Namely, diagrammatic knowledge engages the viewer with the production of meanings. The viewer's interpretation faculty is exercised during diagram-viewing. Thereby passive viewing eventually shifts to active reading, and the viewer is turned into the reader.

At the end of each subsection, I will show how these three arguments can be employed to analyse diagrams of contemporary biosciences (eg. Figure 2.3 and 2.4). Bender and Marrinan argue that the diagrams, be it an *Encyclopedia* plate or Quetelet's statistical graph, function as “working objects”<sup>44</sup>

42 In Wood's thesis, signs are emphasised more explicitly than the meanings represented. However, it is quite clear in his writing that maps unite diverse “sign functions” that represent diverse meanings.

43 The metaphor is that chemical compounds can be synthesised from building bonds between the components. The synthesised chemicals exhibit some characteristics that their components alone do not have.

44 Bender and Marrinan refer to diagrams as embodiments of research process. They cite Daston and Galison (2007) as

in the research process. I will argue in Chapter Five that biological diagrams can be analysed in this aspect and that, importantly, biological diagrams increasingly have these three features because the trends of biological research have shifted toward mechanistic and explanatory accounts. I consider biological diagrams as material embodiments of the research process and that they can be treated as working objects.

### 2.5.1.1 Heterogeneity

Bender and Marrinan's diagrams are material forms of displaying dissimilar things. The sources of data contained in diagrams vary with the ways of obtaining knowledge from the world. The authors survey a wide range of historical means of understanding and representing the world, from the eighteenth-century depictions of object parts in the *Encyclopedia* to Picasso's pixels, then to a contemporary surgeon's helmet that unites various information during a surgery. These diverse means span across different arts and different sciences, where not all of them are visual. For example, the authors discuss Helmholtz's sensory physiology and Boltzmann's quantum mechanics that are barely presented in pictorial forms.

Here I use two examples from this work, an *Encyclopedia* plate and the “surgeon's helmet”, to demonstrate that heterogeneity is a key feature of what the authors call *diagrammatic knowledge*. The distinction between these two examples is seemingly sharp: a contemporary surgeon uses a “helmet” to receive data three-dimensionally from multiple sources during the operation, whereas an *Encyclopedia* plate shows an eighteenth-century agricultural tool and its disassembled parts. The surgeon's experience during the operation is multi-dimensional, involving different three-dimensional measurements through time, while the viewer sees the plate of the agricultural tool as represented in a two-dimensional and static way. However, the authors show that both cases are material forms of representing heterogeneous information and that both forms involve particular ways of uniting such heterogeneity. Both the surgeon and the *Encyclopedia* viewer are offered the opportunity to experience various aspects at once. For the authors, such materialised forms of displaying heterogeneous things belong to *diagrammatic knowledge*. It is clear that through coining this term, the authors do not limit their “diagrams” to visualisations but extend their discussion to non-visual formats of representing knowledge.

Heterogeneity in diagrams not only provides mixed aspects of information but also implies a release from seeing the world from a statically set point of view. While the human visual field has its limitations, diagrams provide a means of configuring multiple perspectives that cannot be simultaneously “seen” in reality. The multiplicity of perspectives embraced by diagrams is, at least in the case of mechanism research, to integrate plural systems of explanations for the same phenomena. As I have addressed in Section 2.1, such multiplicity prevents dominance of any single point of view and is a new way of approaching judgement in contemporary biological research.

The multiple perspectives embedded in diagrams are not necessarily in visual forms. In this regard, Lynch (2014) also maintains that visual representations embody a very wide range of information and embed practices that produce the information. In the case of biological research, both the information and the practices are not necessarily visual until they are translated and transformed to visual representations<sup>45</sup>. For example, many of the perspectives are initially present in the form of numbers and functions (eg. protein structure and ligand-receptor binding kinetics), but eventually they are turned into pictorial forms and gain a role in the viewer's conceptualisation of the abstract

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the source of this notion.

45 See Section 2.6 for my thought (based upon the link between Lynch and Bender and Marrinan) about translation and transformation of both visual and non-visual data to diagram components.

ideas. Taking Figure 2.2 as a demonstration, this diagram is typical in terms of both style and composition, as seen in numerous illustrations of the Krebs cycle (also known as citric acid cycle). Its style is relatively simple, containing only arrows and symbols (ie. the words and the lines together constructing chemical formulas in a standardised format); its composition arranges these visual elements in a circular manner, visually presenting the feature of a biochemical “cycle”. The biochemical information conveyed in this diagram, however, is non-visual in its original form. Only when the biochemical data have been translated and transformed to these symbols, arrows, and the circular arrangement, the viewer is invited to conceive the Krebs cycle with visual references to the circular pathway and the locations of the chemicals within the cycle.

The impressively wide range of diagrammatic knowledge is shown in Bender and Marrinan's historical narratives. They treat very different activities in human culture as diagrammatic knowledge, for those activities are (in their sense) ways of configuring multiple perspectives. As mentioned above, the configurations need not to be visual. For example, they argue that the theatre can be seen as diagrammatic, where visual and audio perceptions act altogether to compose the audience's experience. Statistics can be viewed as diagrammatic, too, for it handles large quantities of complex data with probabilities and makes predictions about complex phenomena. Compared to the theatre and statistics, the diagrams analysed in this study are less radical and straightforwardly “diagrammatic”, for they are two-dimensional and pictorial. However, the complexity and richness of perspectives embedded in these diagrams are not at all less than the art and scientific works surveyed by Bender and Marrinan.

Figure 2.3 is a typical example of configuring heterogeneous perspectives with diagrams in contemporary biology. In Bender and Marrinan's language, this diagram can be described as a visual configuration of “discrete packets of dissimilar data” (Bender and Marrinan, 2003). While this image is indeed two-dimensional, the actual dimensionality of the narratives and explanations is just as complicated as the surgeon's experience within his helmet (see above for Bender and Marrinan's example in their chapter one and six, 2010). Figure 2.3 is a schematic diagram illustrating the mechanistic model of apoptosis (the focused field of this study). The constituent elements of this diagram, such as the mitochondria icon, the arrows, and the geometric shapes, are ostensibly multiple and heterogeneous. But it is the multi-perspectivity represented by these visual elements that really underpins the diagrammatic feature of this visualisation. The heterogeneity of perspectives represented by this diagram is obvious in many senses: the historical times of discovery, the technologies and techniques of discovery, the levels of study (eg. cellular and macromolecular), and the research sites across different geographical spaces and cultural settings. Some of the visual elements (the arrows) represent the directions of biochemical reactions, which are studied by immunological (protein level) and molecular (nucleic acid level) methods. Some elements represent cell organelles, which were discovered by cytological methods. The mitochondria icon is specially designed and represents the inner mitochondrial structure recognised under electron microscope in the middle twentieth century. Meanwhile, another special icon represents a very simplified structure of the proteosome, which was determined by X-ray crystallography in the mid-1990s.

Information represented in biological diagrams is usually retrieved from different and distributed systems of practice, and the research interests and values of those systems are meant to be heterogeneous. In Figure 2.3, data packed with dissimilar methods at scattered places in different periods are visually configured altogether to tell a mechanistic story—through a united multi-perspectivity—of a cell phenomenon<sup>46</sup>. Such visual configuration not only amalgamates the components but also builds relationships between them. Through this relationship-building process, new meanings of the wholes are produced and only present when the component relationships exist.

46 This model is about the interplay between apoptosis induced by death receptor stimulation and survival induced by growth factor receptor stimulation.

Bender and Marrinan have named such relationship-building and meaning-producing processes “correlation”. In next subsection, I will review this concept, while calling it *synthesis*.

### 2.5.1.2 Synthesis

Diagrams are about synthesising dissimilar packets of data through building relationships between them. When the components of diagrams are present alone, they do not make the same sense as when they are correlated to one another. Bender and Marrinan call such a relationship-building feature of diagrams “correlation”:

Correlation is a search for relationships among variables, and its success is measured when a convergence of data is recognised. (2010, 17)

Their analysis of *Encyclopedia* plates shows that making diagrams is an advantageous strategy to convey complicated and heterogeneous messages, as those plates are able to display concepts represented in different formats. But the diagrams' capability of conveyance goes beyond merely representing different things at once. More importantly, diagrams are coherent fields of knowledge, where different representational signs (in Wood's study of maps, a roughly parallel term is “sign function”) and represented concepts are associated with each other. Bender and Marrinan study various pictorial and non-pictorial means of correlating information: from the white spaces linking different images in *Encyclopedia* plates, to Quetelet's visualisation of statistical data in social science, and even to Helmholtz's numerical understanding of sense. Just as heterogeneity of information characterises what the authors call “diagrammatic knowledge”, correlation between heterogeneous components also characterises diagrams, even though such correlation is not necessarily visualised. The authors argue that probabilistic mathematics has a common feature with diagrams (eg. the *Encyclopedia* plates), for both are means of building relationships amongst a quantity of dissimilar data. Both means, while in very different forms, make the “whole” meaningful and only meaningful when the component relationships exist.

Thus the whole is something *new*. In this sense, Bender and Marrinan argue that diagrams are not representations of anything composing them but *presentations* of themselves. While diagrams contain parts that represent dissimilar things, they as wholes do not represent particular referents. A diagram is what it is as a whole, not merely a blend of its components. Diagrams present the new meanings generated through systematic correlation of their heterogeneous parts. In Section 2.5.2, I will link this idea of new meaning presentation to the notion of *supersigns* in Wood's thesis of cartography. Briefly, a supersign is an image composed of dissimilar signs, and the new meaning of the supersign is developed through establishing relationships amongst the component signs.

Based on the linkage between Bender and Marrinan and Wood, I suggest using the term *synthesis* to refer to the process of producing new meanings of the wholes through building relationships amongst the components. Synthesis means that the richness of information of the new whole is greater than the sum of the components. Such a synthesis is reversible, as the component signs and concepts can still be read separately. Uniting heterogeneity is only the first step to the generation of diagrammatic knowledge, and the key step is making the heterogeneous things meaningfully correlate with each other. Chapter Five will show with cases that the new wholes are enabled by the relationship-building process to narrate and explain things.

Signs play an important role in such a process. Bender and Marrinan extensively explore the forms of signs that can correlate between abstract and material ideas, and even between reality and imagination. The white spaces used in the *Encyclopedia* are good examples. White spaces tend to be neglected in pictures, but art historians recognise their signifying functions. Although those white spaces are seemingly the same “blankness” on the pages, they have quite different meanings when

acting to correlate ideas in different contexts. Bender and Marrinan view such white spaces as also constituent elements of the imagery, for such blankness indeed means special things in particular contexts and “unites the plates to one another” (2010, 51).

An example from the *Encyclopedia* shows the role of correlating blankness between signs in synthetic diagrams. In a series of representations of agricultural tools, the white spaces are impressive in terms of their diverse meanings and correlating function. This series starts from illustrations of the tools being placed in a semi-realistic environment. Then the viewing moves toward more detailed and smaller parts of the disassembled tools. Those parts are “placed” in imaginary places, where the realistic painting (such as the use of shadows and highlights) also becomes less obvious. The scales of the parts vary in different illustrations and are not compatible with the illustrations of the whole tools. The points of viewing vary, too, in different plates. In sum, this series of plates opens an array of dimensions, scales, and perspectives, even though this group of illustrations exhibits a continuity in terms of referring to the same agricultural tools. Here, two kinds of signs crucially contribute to this continuity: the consistent numbering of the tool parts, and the white spaces that shift the viewer's attention from real-world concepts to imaginary ideas. The numbering of tool parts serves the consistency of reference, and the white spaces release the viewing from a single point through gathering a “system of perspectives” (2010, 13). In the plate of the whole tools, the white space is a part of the semi-realistic environment, possibly representing the field or the sky or other real landscape. In the plate of disassembled parts, the white space is an entirely imaginary background for displaying the objects. Neither case treats the white space as a meaningless void. These two kinds of signs (numbers and white spaces) *synthesise* all the illustrations and turn them into a new coherent field of diagrammatic knowledge.

Contemporary biological diagrams normally (or always, if in the case of mechanism diagrams<sup>47</sup>) possess this synthetic feature. I here use Figure 2.4, a textbook diagram illustrating the mechanism of activating a transcription factor nuclear factor kappa B (NfκB), as another typical example of contemporary biological diagrams. This diagram exemplifies how the uniting of heterogeneous information and signs is made sense of through a relationship-building process. Some of the component signs are general graphs widely used in countless places, eg. curves, arrows, and lines, and they are imposed specific meanings in this diagram, eg. biological entities (cell and nuclear membranes) and activities (phosphorylation and ubiquitination). Some of the component signs are specially designed for particular things, such as the signs of NfκB and IκB complex. As mentioned in Section 2.5.1.1, biological diagrams tend to synthesise discoveries spanning a long historical time and across a range of research areas. The “pore” structure of the nuclear membrane is a long-established concept in cytology, and it is schematically represented with very simple iconographic elements. This “nuclear membrane” is not even wholly drawn, but the informed viewer can interpret this conventional depiction. The NfκB complex sign is not as conventional as the sign of nuclear membrane, not only because the structure is a novel discovery but also due to the possible ambiguity caused by the high degree of simplification. Figure 2.5 presents the structure of this complex. Although this “ribbon” structure is still simplified, it contains more information of the structural units and is detailed enough to be contrasted with Figure 2.4. Comparing Figure 2.4 and 2.5 also suggests that the NfκB icon in Figure 2.4 indeed resembles the actual structure.

The synthesis in Figure 2.3 forms a new array of knowledge that is “impossible to infer from any single element” (Bender and Marrinan, 2003). For example, the uniting of different things is meaningful in Figure 2.3 because it imposes diverse meanings on arrows and white spaces, which together compose the environment for the cellular dynamics: the white spaces represent both extra- and intra-cellular spaces, and the arrows represent various activities that are either sequential

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<sup>47</sup> Mechanism diagrams are treated as a type of biological diagram in this thesis. There are other types, such as object drawings and experimental design. Chapter Three shall introduce my taxonomy of biological diagrams, and Chapter Four and Five will explore in detail the features of some major types.

(involving time) or directional (and perhaps causal). The arrows are especially the key element of making correlations between the other heterogeneous elements. While the arrows are in some senses imaginary (compared to those icons of entities), they represent the actual actions between the entities and appear together with the icons of tangible things. These arrows and white spaces are just like Bender and Marrinan's white spaces and numbering in the *Encyclopedia* plates of agricultural tools. These iconographic connections between heterogeneous parts provide visual consistency, building relationships between the initially-fragmented messages. Without the presence of the arrows, the special NfκB sign can represent other protein complexes, and the meaning of "nuclear membrane" sign can be ambiguous. Because of the relationships built by the arrows and the white spaces, they are now parts of the coherent array of signs.

It might be noted that, however, only the informed reader recognises the plural meanings of the arrows and the white spaces. The reader without trained judgement is not able to distinguish the arrow representing "cytokine stimulation" from the arrow representing "ATP being dephosphorylated to ADP" arrow, especially because the arrows in this diagram have the same appearance. In other words, the informed reader is more capable of deciphering these visual codes and interpreting the meanings and even the contexts of discoveries (such as the employed technologies and the research interest of the areas). The informed reader, in this regard, is more *engaged*. Moreover, if the informed reader is a practitioner of related fields, s/he will probably get back to the real-life practice with influence from the knowledge in this diagram. In the case that the informed viewer is a researcher of any perspectives represented in this mechanistic model, this diagram functions as a tangible "map" for contextualising one's own research in the network of knowledge. In such a case, the engagement is beyond interpretation and extends into the real life of the viewer. This is comparable to Bender and Marrinan's argument about engaging the viewer of a painting or the audience of a theatrical play. Eventually, the diagrams become the medium for not only preserving and conveying but also materialising and examining theories and extrapolations. In next subsection, I will review how diagrams become working objects in the research process through engaging the viewer.

### 2.5.1.3 Engagement

The third argument extracted from Bender and Marrinan for my analytical framework is *engagement*. This study distinguishes the condition of engagement in biology from art history. The last paragraph of this subsection and Section 5.6 will both explore that engagement of the viewer in biology does not concern one's self-projection of personal affections onto the artworks (as in art history) but one's real-world practice within the wider research community.

In Bender and Marrinan's thesis, the notion of engagement is mostly developed in their review of the history of theatre, in terms of architectural design and the form of display. It should be noted here that, while the theatre contains human acting and the affections of the actors, Bender and Marrinan have a reason to treat the theatre as a kind of diagrammatic display like the *Encyclopedia* tableaux. In the history, the distinction between the acting and the audience has been either sharpened by an imaginary boundary (the "fourth wall") as proposed by Diderot or crossed by a "demi-illusion" as proposed by Marmontel. Although the latter case appears to imply an emotional interaction between the actors and the audience, the audience is actually aware of the fictional feature of the acting and that the actors are not affected by the response from the auditorium. Such a relationship between the audience and the device of theatrical displays in some senses is comparable to the viewer perceiving two-dimensional and static paintings. The main points are that the theatre is also an embodiment of the culture of diagram and that, importantly, it is an exemplification of engagement.

The theatre configures heterogeneous sources of perceptual stimulation in a multi-dimensional way, namely, a “diagrammatic” way. Such a configuration unites the audience who has heterogeneous backgrounds through arranging the audience in a set auditorium and an “interactive shaping of affect” (2010, 114). This configuration also unifies the emotional response of the audience. The diverse audience is turned into a collective whole, for the configuration of perceptual stimulations (eg. the sound, and the poses of the actors) incites a shared interest amongst them. The diverse audience is motivated to reflect their own experiences on the same device of displays. That is, the audience is *engaged* in a united way so that their self-projections are unified. This engagement brings diverse subjectivity to a common experience, even if the subjectivity is as diverse as from “a thousand souls” (2010, 111).

Then it is clear that, to make the diagrams persuasively powerful, building relationships amongst the constituent elements alone is not enough. Based on Bender and Marrinan, I suggest that the engagement of the viewer is central to turning a representational diagram to a presentational visual discourse that has impact upon real-world practice (the next section on Wood shall explore this aspect). Thus the viewer of diagrams is eventually the *user* (Bender and Marrinan's term). They maintain that the user does not passively view the diagram but gets involved in the process of generating diagrammatic knowledge via self-reflection of their own subjectivity onto the images. The authors use Shapin and Schaffer's notion of “virtual witness” (see Shapin and Schaffer, 1989) as a ground for arguing about diagrams being systems of persuasion. The notion of virtual witness comes from natural philosophers' trust in the reliability of testimony of scientific phenomena based upon the multiplication of witnesses, both directly and indirectly. The experiment, the report of the experiment, and the underlying technology can all be parts of the system of persuasion. These parts serve to propagate and extend the witness experience. A system as such may be described as a medium for inter-subjective exchange, and diverse perspectives are united into a system of “multiple points of attention”. This resonates with Bender and Marrinan's argument on “dispersed vantage points characteristic of the plates of the *Encyclopedia*” (2010, 154-55). Especially in the realm of science, such a medium for exchanging subjectivity can be persuasive. The user is required to actively exercise one's faculty of interpreting the message and reflecting on one's real-life research.

Unlike some of the art works studied by Bender and Marrinan, biological diagrams are not meant to incite emotional reactions. Nor are they supposed to be connected with the researchers' private affections. Nonetheless, biological diagrams are really the media for inter-subjective exchange and multi-perspectivity formation. The dispersed perspectives from different research areas are integrated in the diagrams. This concept corresponds to the inter-field integration in biological mechanism research discussed in Section 2.4: the user actually uses biological diagrams as maps to contextualise one's own discoveries. The researchers work between the diagrams and the laboratory bench, just like Bechtel's (2006, 61-2) description of the process of searching cell mechanisms through modelling, revising the explanations, and adding new extrapolations (both are *presented* by the diagrams). Here, the status of diagrams as working objects is obvious: they are the “materials from which concepts are formed and to which they are applied” (Daston and Galison, 1992, as cited in Bender and Marrinan, 2010, 33).

### 2.5.2 Wood (1992; 2010)

This section focuses on Wood's notions of sign systems and the relationships built between them, instead of his interest in the social implications of the power of maps. Neither will this section discuss other cartographic sources that point out the power relations embedded in map-making. This is because this thesis deals little with the social aspects of visual representation. Nonetheless, as this



section shall introduce, this thesis still will reveal the engaging power and the pragmatic aspect of biological diagrams in terms of the user's intervention in the physical world. Through engaging the user, biological diagrams actively participate in the making and re-making of what they represent, and thus blur the distinction between the representation and the represented. In cartography, a comparable status of maps has been mentioned in Wood's thesis and argued by some sources of critical cartography since the middle 1990s<sup>48</sup>. The discussion of this thesis will show that biological diagrams are similar to maps, in the sense of constantly being in the “state of becoming” (Dodge, Kitchin and Perkins 1999, 18) that interweaves the practice of exploring reality and the making/re-making of representation (Section 5.6.4). Now this section starts introducing the use of cartography with the comparability between the sign systems in maps and biological diagrams.

Wood argues for four levels of the “signing process” of maps, which are consistent with the three arguments I extracted from Bender and Marrinan (the previous section). This is not to say that Wood's maps entirely belong to Bender and Marrinan's broad category of diagrams, but that the overlap between these two sources provides a productive means of understanding particular *synthetic* kinds of images (which surely include contemporary biological diagrams).

Wood's first level of maps generating and structuring their signing process (2010, 98) is “elemental”, namely the visual elements in the language used by Bender and Marrinan and this study. The second level is “systematic”, which requires the relationships built amongst the elements. In Bender and Marrinan's terminology, such relationships are called correlation. The third level is “synthetic”, where the new meaning of the image as a whole is generated. From this level, the whole construct can be treated as a *supersign*:

At the synthetic level... dissimilar systems enter into an alliance in which they offer meaning to one another and collude in the genesis of an embracing geographic icon.... This is the map image. (2010, 98)

The fourth level is “presentational”, where the supersign (ie. the map image as a whole) is read together with its “perimap” surrounding it. The perimap may include various kinds of information. Wood argues that this level is when interpretation of maps is brought back to the contexts of production and use, and when maps acquire their discourse<sup>49</sup> functions. At this level, maps are capable of presenting propositions and engaging the users in real-world practice.

Wood emphasises the relationships amongst different layers of component signs contained in maps as greatly as Bender and Marrinan emphasise the correlation amongst visual elements in diagrams. I consider that these two arguments point to the same crucial feature: the meaningful and purposeful integration of heterogeneous elements and embedded information. In the above quote, Wood explicitly points out the dissimilarity—which is comparable to Bender and Marrinan's view for the contents of diagrammatic knowledge—of systems incorporated together in the maps. The systems of both sign functions and the concepts conveyed are dissimilar. In my term borrowed from Bender and Marrinan, these are diverse systems of *perspectives* retrieved from different practices. In Wood's concept of maps, such diversity and heterogeneity of perspectives are synthesised by the maps as supersigns, wherein the constituent signs of a supersign “can only have meaning in relation to other signs” (2010, 104).

Wood's notion of “maps as supersigns” acts as a cartographic version of Bender and Marrinan's “diagrammatic knowledge”, as it nicely accommodates the three arguments of Bender and Marrinan (as reviewed in the previous section):

Maps are about relationships. In the even least ambiguous maps, simple presences are

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<sup>48</sup> Del Casino and Hanna (2005) reviews some key literature.

<sup>49</sup> Wood argues for maps as discourse in the vein of Foucault and Barthes. This position is explicit in Wood (2007).

This thesis does not go into the details but focuses on the aspect that maps and biological diagrams are both capable of persuading in real-world practice. Section 5.6.3 will elaborate on this aspect.

absorbed in multilayered relationships integrating and disintegrating sign functions, packaging and repackaging meanings. The map is a highly complex supersign, a sign composed of lesser signs, or, more accurately, a synthesis of signs; and these are supersigns in their own right, systems of signs of more specific or individual function. (1992, 132)

Such a continual and dynamic process of establishing relationships amongst the constituent signs and their meanings—again, which embed heterogeneous perspectives—results in the production of a new meaning of the synthetic supersign. The argument for “supersigns in their own right” finds its parallel in Bender and Marrinan's view for new meanings of diagrams, where they quote Reviel Netz (1999): “The diagram is not a representation of something else; it is the thing itself.” (Bender and Marrinan, 2010, 10)

The signs composing the maps are actually codes, artificially imposed with signifying functions that become meaningful through relationships (ie. Bender and Marrinan's correlation). Wood does mention correlation both between the elements and the meanings and amongst different elements, when he explains the reason for treating signs as not solitary elements but “sign functions”. Wood quotes Umberto Eco's semiotic argument that is slightly radical about naming “sign functions” rather than “signs”:

Properly speaking there are no signs, but only sign functions... a sign function is realized when two functives (expression and content) enter into a mutual correlation; the same functive can also enter into another correlation, thus becoming a different functive and therefore giving rise to a new sign-function. (1992, 109)

Wood's signs are “sign functions” because they are neither the signifier nor the signified. Neither can form a sign when is present alone. A sign only exists in an established correlation by particular coding rules. The geometric shapes in Figure 2.4 could not represent the intracellular molecules, such as Bcl-2 and Bid, if their correlations to their sign functions *and* to other visual elements (other signs) are not established via the encoding of meanings. For Bender and Marrinan, a visual element's correlation with something else is less about the encoding of it (in Wood's sense) but more about its relationship with both other visual elements and the viewer's self-reflection. This difference between the two sources may be due to the difference of angles between art history and semiotics (which Wood employs to study the signs in cartography). Nonetheless, in both sources, building relationships between the elements is unavoidable in the process of making meaningful the image as a whole or a supersign. The white spaces in Figure 2.3 and 2.4 well exemplify the centrality of relationship-building in the making of supersigns. These white spaces are the same visual elements, but they are coded with different sign functions that respectively represent the extra-cellular environments, the cytosol (the intracellular substance that does not include cell organelles), and the inside of the cell nucleus. In this sense, the coding process helps contextualise the two mechanisms in their environments. The same whiteness could not represent different spaces without its relationships to different surrounding components. The surrounding components are the other sign functions, which also act as part of the *continuity* of relationships amongst all the elements and their meanings.

With regard to the encoding of sign functions, nonetheless, I argue that there is a difference between two kinds of supersigns: maps and biological diagrams. The results presented in Chapter Four will show that biological diagrams exhibit much ambiguity in the visual conventions used in their component iconographic elements. In cartography, visual components of a map somehow exhibit much consistency with the other maps in terms of their meanings. Visual conventions in biological diagrams tend to vary case to case and author to author, unless uniformed by the media for publicity (such as a journal). For example, blue curves tend to represent waterways in cartography, although in some maps they represent rivers and in some other canals. But cell membrane in biological diagrams can be represented by a range of different graphs. Chapter Four will show that there is no

fixed standard for creating visual conventions for the visual representations of cell membrane. There can be exceptions, for example, when some journals have uniform styles for visual representation (see Section 4.2.5, where *Nature Reviews Molecular Cell Biology* especially exhibits a uniformity in style). But such uniform styles only technically work within particular journals and do not show much influence on other journals. The point of this difference between maps and biological diagrams is that biological diagrams do not rely on certain degrees of uniformity in their visual conventions to qualify as supersigns. The communicative function of biological diagrams intriguingly transcends the need for visual consistency. Therefore, I speculate that the power of relationships amongst components of biological diagrams acts at a greater degree than map components. The relationships are so central to making meanings of the components that the variety and ambiguity of the components do not interfere with the interpretation process, at least in most cases.

Once a supersign is formed, the map moves on to Wood's fourth level of signing process: the presentational level. At this level, maps have power of doing work to the world, which they simultaneously speak of and speak about (2010, 106). This level is about maps acquiring the position of “legitimate discourse” (2010, 97), when they are organised together with the surrounding “perimaps”. A perimap is “a crowd of signs” provided jointly with the maps. It can be any device of visual expressions and embraces highly heterogeneous information about the contexts of map-making and map-using. I consider the uniting of maps and perimaps as a configuration of maps and their cultural contexts, and that this configuration facilitates the understanding of the conventions embodied in maps. This is why the maps become legitimate discourse at this presentational level—they are now connected to the contexts of their production and ready to *influence* the world when used by the viewer. The viewer becomes the user. In other words, one is *engaged* by the maps in the process of making the images meaningful in a practical way.

Such an active status of the map user parallels Bender and Marrinan's argument on the engagement of the diagram viewer. Bender and Marrinan discuss how the diagram viewer projects self experiences and affections onto one's perception in front of diagrammatic displays. This self-reflection correlates (or, in the language of this thesis, builds a relationship between) the diagrammatic displays and the viewer's real-life knowledge and experience, engaging the viewer in the reading process that is crucial to the generation of meanings of the diagrams. In a comparable sense, Wood's discussion of maps emphasises the engagement of the user in the process of “injecting the map into its culture” (2010, 106). The culture of the map embraces not only the map maker and the map user, who are identified as what Wood calls “percipient”, but also their ability to “generate and utilize the strategic codes” that are formalised by the maps. The user is actively engaged in: (1) generating the meanings of maps and (2) utilising the strategies communicated by maps. Through such processes, the maps are practically associated to and make impact on the world, rather than merely representing it.

Here, activeness and autonomy of the “percipient” of maps stand out to act as the “most prominent aspect” (2010, 106) of maps' discourse function. Wood's argument mentions the map maker and map user separately; while Bender and Marrinan mention the viewer becoming the user of the diagrams but do not elaborate on the producer. According to the practice of making and using biological diagrams, I treat all these three identities as in the same category. Namely, someone who ever views, reads, produces, and makes meanings out of the synthetic supersigns. Section 5.6.4 will elaborate on the multiple roles of the same viewer in biological practice and suggest that this overcomes the problem of producer-user dichotomy in cartography.

The reading process of synthetic supersigns, in both cartography and art history, is not passive but actively interpretative and (sometimes) utilitarian. In biology, the reader of Figure 2.3 or 2.4 not only perceives the dynamics of the cell mechanisms but also conceives the research background through reading the relationships amongst the signs. Moreover, as described in the end of Section

2.5.1.2, the reader utilises these diagrams to contextualise one's real-life practice in the network of collaborative research. Just like maps enter the social realm of their culture through engagement of the “percipient”, biological diagrams enter their culture through the reader utilising them as working objects, which embody the research process and make legitimate discourse (in Wood's term) that shapes future research (this idea will be discussed in Section 5.6.3).

## 2.6 Photo-diagram relationship: Lynch (1990; 2014)

Given the little attention paid to scientific visualisation in the 1980s and early 1990s, Lynch's study on diagrams serves my analytical framework with a ground-breaking argument on the sophisticated process of transforming photographs to diagrams in biological practice. Lynch elaborates on the process of making transformative “renderings” (1990, 160) from photographs to diagrams, arguing that such transformation requires more deliberate manipulation than simplification and schematisation of the details in photographs<sup>50</sup>. This section will also show that his thesis serves as a start rather than an end of capturing the richness of diagram-making in biological practice and its implication.

This work is a great start because it argues for the theory-ladenness of diagram-making and shows with concrete examples (eg. Figure 2.6 and 2.7) how photo-diagram transformation embodies the intention of scientists to communicate theories. Also, it is a start because it touches some other kinds of biological diagrams (eg. Figure 2.8) that exhibit less or no resemblance to any specific photograph. Those diagrams are to convey multiple aspects of biological concepts. With regard to using Lynch's thesis as a start, the other point important to this study is clearly maintained in the latest version (2014) of Lynch's viewpoint for visualisation in the era of digital information. This point implies the status of visualisations as working objects in scientific research:

To put this [the fact that visualisation in science is not always about something “visual”] another way, visualization includes the arrangements of materials, instruments and their outputs, and the embodied practices that *produce* visual display. The literary end products may be visual and graphic, but the technologies through which “raw data” are processed often operate quite differently from the mind's eye (or the eye's mind). Visualization is as much the work of hands — often many hands — as it is of the so-called “gaze.” (2014, 325)

This passage nicely shows that scientific visualisations: (1) can be synthetic constructs of heterogeneous formats of data *and* data-generating means that are not necessarily “visual” in the first place; (2) are the embodiments of these heterogeneous things through certain processes of translation and transformation. This point also implies that visualisations serve as materialised forms of perspectives, for the “gaze” is made concrete and visual through the translation and transformation. In Chapter Four and Five, this point shall be revealed as a significant feature of biological diagrams.

On the other hand, Lynch's study does not fully explore the still richer contents of biological diagrams. For example, visual items similar to Figure 2.3 and 2.4 are prevalent in a range of contemporary biological areas. But Lynch's study (including both his 1990 paper and his latest thesis of revisiting scientific representation, 2014) does not reveal this kind of visibility as deeply as he does to the “resemblance” kind of diagrams. Although Lynch's 1990 paper proposes a term “mathematization” to characterise the purposeful addition of some visual elements (such as scales) to diagrams, this term seems not fairly adequate to describe the actual features of diagrams containing non-resemblance elements. This is because the added, non-resemblance elements have

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<sup>50</sup> Here, Lynch's “rendering” is sometimes read and used as a noun, referring to the diagram; sometimes it is read as a verb, referring to the process of rendering diagrams.

far more than just one category of meanings. That category, in Lynch's viewpoint, is to “mathematize” the visual objects drawn from photo-diagram transformation. However, biological diagrams that employ visual elements like scales do not necessarily deal with mathematics.

This limitation of Lynch's study of diagrams is perhaps due to a “time difference”. The complexity of biological diagrams, as well as the prevalence of complex diagrams (eg. Figure 2.3 and 2.4), have drastically increased since the 1990s (such trends will be revealed in Chapter Four and discussed in Chapter Five). It is thus not surprising that Lynch's relatively earlier study (originally published as a journal paper in 1988 and then a book chapter in 1990) does not capture the yet-upcoming features of emergent diagrams. His 2014 book chapter still does not explore much the complexity of recent diagrams, as the book concentrates on the relationship between practice and representation in the digital era. But I suggest that Lynch's study is still helpful to characterising some diagrams that do not have one-to-one transformative relation to specific photographs, for his study on the “modelling” kind of diagrams has a hidden link to Bender and Marrinan's notions of synthesis and multi-perspectivity (see Section 2.5.1). Later in this section, I will review this link.

Lynch argues about photo-diagram relationship by presenting a “split-screen” format (Figure 2.6 and 2.7) of displaying photographs and diagrams at once. He considers the process of making diagrams from photographs as directional (1990, 200) and that this process requires not only reduction but also selection. During selection, visual elements are added so that the diagrams represent information that was once incomplete, unclear, unidentified, or to be extended in the photographs. In both Figure 2.6 and 2.7, the two bottom diagrams appear to be resemblances to the two top photographs, and these “resembling diagrams” appear to be just the schematised and simplified version of the photographs. But these two bottom diagrams in fact contain information that is not possibly seen in their “reference” photographs. In Figure 2.7, the diagram even presents a rotated version of the object captured in the top photograph and contains three-dimensional painting of structural information about the object. These two diagrams are examples of directionally transformative renderings. Lynch considers photo-diagrams relationship in biological practice as not only “sequential in time” (1990, 160) in terms of their production but also a “rendering” that irreversibly alters the content of the captured images.

Lynch discusses two types of transformative rendering from photographs to diagrams. One type is about producing a photo-diagram pair through one-to-one transformation. The other is making a diagrammatic model that is not directly bound to any specific photographs. In the making of the former-type renderings (eg. Figure 2.6), these steps take place:

- ⤴ Filtering: the screening process that excludes undesired noise and uneven background.
- ⤴ Uniforming: eliminating the variation of important details through artistic manipulation.
- ⤴ Upgrading: highlighting particular characteristics that define the key details.
- ⤴ Defining: making different parts more distinguishable from one another than in a photograph.

Both “upgrading” and “defining” transform the entities represented and make them relatively definite in terms of their unique features, while “defining” sometimes requires adding verbal tools (such as numbers and abbreviations of names of the parts). On the other hand, “upgrading” the entities can be about emphasising the continuity of the borderlines of specific parts.

The other type of rendering models biological phenomena or objects. A model diagram (eg. Figure 2.7) is not tied to any specific photographs but offers a generic concept of the object from various aspects. Lynch maintains that such models “transcend the perspectival limits of the photographs” (1990, 167). Thus the observation of the object is freed from a single angle of view. Such transcendence echoes with the freedom of perspectives that Bender and Marrinan (see Section 2.5.1) assume to be a characteristic of diagrammatic representations. Lynch's notion of such multi-

perspectival representations involves imposition of ideas. While a model diagram contains elements that are from empirical data (just like the three-dimensional structure in Figure 2.7), it is an imaginary re-assembly of the biological phenomenon or object that cannot be exhausted by any single one of the empirical practices embedded in it. Such a diagram displays a convergence of fragmented parts resulting from analytically disassembling the object (1990, 167). This convergence, owing to the multiple perspectives it contains, provides a more comprehensive understanding of the phenomenon or object than any single photograph can offer.

Lynch's "mathematization" is relatively vague compared to his argument about transformative rendering. This is probably due to a confusion between mathematics and orderly, analytical means of displaying information. Lynch considers diagrams as more faithfully representing the hidden order of natural phenomena than photographs, for some diagrams (eg. Figure 2.8) are imposed with higher "measurability" (Lynch's language) via addition of particular visual elements. But Figure 2.8 is actually an example of the inadequacy of this language. In this diagram, the dotted lines represent different sites and angles of brain-sectioning. These lines help explain the source of the presented brain slices. The small diagrams of brain slices are resemblances to the actual things and are produced from transformative rendering. The dotted lines and the correlating white spaces are imaginary elements organising the information about the brain in an orderly way that does not exist in nature. One may argue that such an ordered organisation can be used for some sort of measurement. However, I cannot totally agree with using either "mathematization" or "measurability" to characterise this representation of brain-sectioning. Although the sectioning as a technique in the real world might require computerisation, the representation per se—as shown and discussed by Lynch—has nothing to do with numeracy.

In fact, Lynch's notion of "measurement" is not used in a common mathematical sense but originated from Heidegger's *mathesis universalis* (1990, 162). This specific sense of "mathematization" frames natural phenomena in graphic spaces that are artificially organised with order. Thereby scientists can analyse the order of the phenomena. Lynch terms such an analysis "mathematical", but this terminology runs a risk of inviting confusion and controversy in common contexts of mathematics. Meanwhile, measurability is not necessarily (in fact, normally not) the purpose of adding descriptive or explanatory visual elements to biological diagrams. Although diagrams of cell mechanisms can represent both spatial and temporal orderings of the component relationships (Section 2.4 has reviewed the advantages of diagrams in representing such orderings), such orderings normally are not for quantification. Instead, this study will show that most biological diagrams containing information about order are not subject to "mathematical operations" (1990, 163). Therefore, one must be careful when adopting Lynch's "mathematization" and "measurability" to characterise biological diagrams, for this terminology should be clarified by referring to Heidegger's concept of mathematical universe.

Instead of adopting the term "mathematization", I consider such a characteristic as an appeal to orderly and analysable frameworks for treating diagram components. This appeal relies on transformation and translation from data to diagram components so that the ideas conveyed become analysable. The analysis can be either quantitative or qualitative and is likely to be structural, logical, and highly mobile across different research cultures. Again taking Figure 2.8 as an example, the added lines and measurements are to communicate the structures of the specimens in a somewhat standardised way. My notion of such an appeal captures Lynch's emphasis on order and the analysable aspect, while avoiding confusion with quantitative incentives.

I consider transformation and translation as also required in the visualisation of data that is not "visual" in its original form. This fits in Lynch's 2014 thesis on the diverse forms of data produced by novel technologies (see above). By using the aforementioned link between Lynch's 2014 thesis and Bender and Marrinan's argument (2010), I have suggested that the visual components in diagrams come from heterogeneous sources that are very diverse in terms of visibility—and some of

the sources were not visual items at all. Transformation and translation act to convert such heterogeneous information to visuals. But even in this sense, the relationship between data and diagrams is not one-way directional as Lynch argues. This study will show that the transformation and translation of data to diagrams are more complex (Chapter Four and Section 5.2). They not only change the formats and styles of data but also can change the epistemic roles and signifying functions of it (Section 5.5.3).

## 2.7 Conclusion

I conclude this chapter with a summary of the connections between the sources reviewed (next paragraph) and a plan for employing the analytical framework they together construct (the third paragraph).

This chapter has reviewed the main sources that contributed to the analytical framework of this thesis. Daston and Galison (2007) has linkages to the other sources in terms of the plurality of the ideas about “right depiction”, images-as-presentations, and utility of images in scientific-engineering convergence. Also, the other sources are inter-connected. Some of the connections are about supporting each other, and some are about being complementary to each other. Section 2.2 explored the autonomous function of visual representations in different disciplines through reviewing Rudwick (geological sciences), Ferguson (technology, 1977), and Gooding (physics, 1990). This autonomy plays a role in both communication and conceptualisation of science and technology. Section 2.3 reviewed Rasmussen's history and philosophy of electron microscopy, showing the role of images as the interactive media for integrating diverse practices. Section 2.4 reviewed Bechtel and Craver and Darden, who are important authors in philosophy of biological mechanisms, yet this section specialised in reflecting the features of biological mechanism research on visualisation. Section 2.5 maintained three key notions of this study, based upon Bender and Marrinan and Wood: (1) heterogeneity, as paralleling the concept of diversity of perspectives argued by Rasmussen, Craver and Darden, and Bechtel; (2) synthesis, as paralleling and supporting Craver and Darden and Bechtel in terms of inter-field and inter-level integration; (3) engagement, as extending Daston and Galison's “new images” that simultaneously engage the user and serve as tools for intervention in real-world phenomena. Finally, Section 2.6 reviewed Lynch's argument on sequential transformation from photographs to diagrams. This section proposed to extend his thesis to a richer analysis of novel and complex diagrams, which his 1990 work does not cover.

Chapter Three will introduce my methodology established based on this framework. Chapter Four will present the results from the analyses. Chapter Five will discuss the results by applying the key ideas of this framework. The results extend and support some of these key ideas, while revising some others. Chapter Six as my conclusion will show that this study fills in three gaps in the existing scholarship and that biological diagrams embody the key components of this framework.

## Chapter Three: Methodology

### 3.0 Introduction

This chapter presents the methodology of this study. The collection and analysis of data will be presented in Chapter Four, and the discussions are in Chapter Five. The methods were used to analyse published diagrams in biological papers. This study defines *diagrams* as belonging to *visual items* in papers. **Visual items** (abbreviated as **VI**) are items put in any visual format separate from the text, where tables are excluded. **Diagrams** are visual constructs that can convey synthesised information or represent entities, experimental design, and mechanisms. This definition excludes data images obtained from experimentation and simulation<sup>51</sup>. This definition has similarities to, but does not follow, Kemp's classification (1997) of some sorts of scientific images<sup>52</sup>.

The overall methodology aimed to analyse a population of diagrams at a statistically meaningful scale. Eight journals were selected according to their contributions to the knowledge of apoptosis. The sample size was determined as statistically representative of the population. The results (which Chapter Four will present) were from a survey on 3,512 papers and an analysis of all diagrams they contain. Results were divided into two parts, quantitative and qualitative, and discussed jointly in Chapter Five. The quantitative part analysed the comprehensive patterns of coverage of the diagrams, and the qualitative part analysed the contents of diagrams in terms of components and contexts.

### 3.1 Selecting journals and collecting papers

Journals and papers were selected via the following steps. Firstly, a preliminary survey was conducted on most-cited papers and significant findings in apoptosis research during the period between the launch of apoptosis concept (circa 1972) and 2005. This step used a scientometric survey of the growth of apoptosis field between 1972 and 1996 (Garfield and Melino, 1997). From their study, I compared and extracted key publications from three tables of citation ranking: most-cited journals, most-cited papers, and most-cited authors. Some highly specific journals were excluded because of their relatively narrow scopes, such as journals concentrating on the digestive system (*Gastroenterology*) and haematology (*Blood*).

Secondly, journals containing landmark discoveries are selected based on historical reviews written by apoptosis researchers (for example, Vaux, 2002). This not only extended Garfield and Melino's survey (1997) from 1972–1996 to 2005 but also recognised the far-reaching discoveries

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<sup>51</sup> This thesis defined visual item, diagram, and mechanism diagram in 2011, when my survey started. Coincidentally, my definitions for “diagrams” and “mechanism diagrams” are largely in harmony with Bechtel et al. (2014), where they define scientific diagrams as “visuospatial representations” and mechanism diagrams “graphical representations of the parts and operations of a mechanism” (2014, 164). The distinction between my definition for diagrams and theirs is that theirs includes some data images, such as line graphs. Their discussion does not cover diagrams representing experimental design and biological entities (without activities). Section 3.2.2 will provide my categorisation.

<sup>52</sup> However, this study does not follow Kemp's classification of scientific images. Kemp divides scientific images into depictions of subject matters and illustrations of “science as a pursuit”, but the materials surveyed in this thesis contain only diagrams of, or related to, the subject matters of scientific investigation. Also, biological diagrams are not always depictions. They may have quite remote visual relations to the objects of interest. Moreover, diagrams may incorporate representations obtained directly from experiments. All such variations make Kemp's classification unsuitable for this study.



acknowledged by practitioners in this field. Thus the importance of the selected papers is both quantitative and qualitative. In the apoptosis field since the 1980s, molecular and cell biological discoveries tend to make significant contributions. This led to my inclusion of a young yet influential review journal on molecular and cell biology (*Nature Reviews Molecular Cell Biology*).

These are the eight journals selected:

1. *Journal of Cell Biology (JCB)*
2. *Proceedings of the National Academy of Sciences of the United States of America (PNAS)*
3. *Cell Death and Differentiation*
4. *Nature Cell Biology*
5. *Nature Reviews Molecular Cell Biology*
6. *Cancer Research*
7. *Cell*
8. *Federation of American Societies for Experimental Biology (FASEB) Journal*

*Cancer Research*, while not specialising cell biology, is selected not only because of its high ranking but also, more importantly, due to the close connection and obviously overlapping interests between cancer research and cell death<sup>53</sup>. Section 4.2.6 will show that this journal actually published more apoptosis papers than some of the cell biology journals.

Once the journals were chosen, two keywords were used to identify relevant papers: “apoptosis” and “cell death”. The reason for using two keywords was to capture as many papers relevant to apoptosis research as possible, for sometimes apoptosis researchers do not distinguish these two terms in their writing. Some papers even take for granted that necrosis is another kind of cell death. The date range of search for each journal slightly varied. Some journals had not been established until the late 1980s or the 1990s. For journals established earlier than 1980, 1972 is normally set as the start point of search. This year is when the researchers deliberately identified the morphological and (patho-)physiological distinctions between programmed cell death (apoptosis) and necrosis (see Chapter One). The endpoint of the date range is set 2005 for all journals. The numbers of samples in the 2000–2005 period satisfied the need for representative quantification. Because of the exponential growth of apoptosis papers since 2000, this endpoint ensured the ease of data-handling.

To locate relevant papers in the archive, keywords were searched in two fields: *title* and *abstract*. This strategy is a modified version of an existing method used by some scientometric studies, such as the aforementioned survey of apoptosis field (Garfield and Melino, 1997) and a survey of the evolution of STS discipline (Martin et al., 2012). The existing method only searches for keywords in the titles and can miss important papers, for scientific papers do not necessarily put keywords in the titles. Such a methodological flaw of publication mining is mentioned by Martin et al. (2012). Previous methods for identifying thematic orientation of academic publications focus on the title<sup>54</sup>, assuming that the themes are reflected by the keywords in titles. But the most relevant keywords may only appear in the abstracts or the text. This is the case not only in STS publications, but also in biology. Especially in apoptosis field, scientists may take for granted that “cell death” actually includes both apoptosis and necrosis. This study eliminated this methodological flaw.

But this improved strategy for search was so inclusive that it could fail to omit papers not directly relevant to apoptosis research. This problem was solved by a purely manual process of checking the

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<sup>53</sup> To briefly explain the link between apoptosis and cancer research, carcinogenesis can result from the imbalance between apoptosis and cell survival. This is because apoptosis helps maintain homeostasis in healthy individuals. Therefore, interest in cancer therapeutics normally has a close interaction with the study of apoptotic mechanisms.

<sup>54</sup> Another example is a survey on innovation study by Fagerberg et al., 2012

contents of papers returned by the search. For example, a paper examining cell differentiation may observe apoptosis in cells that fail to differentiate. Such an observation is very likely noted in the abstract, while no experiment is designed to investigate either the cause or the effect of the observed apoptosis. In such a case, apoptosis is merely an indicator for undifferentiation, not the object of enquiry. The manual screening criteria are based upon: (1) first-hand laboratory experience in molecular and cell biology of apoptosis, cytotoxicity, inflammation and cancer, and (2) a survey on biomedical literature. This manual process also omitted erratum, retractions, and duplicates whilst removing papers on irrelevant topics.

The sampling of papers was conducted in tandem with this screening. The search returned a large population of papers. In most cases, the populations from the journals are too large, practically, to study in their entirety. A decision was made to sample the papers to ensure statistical significance of the dataset. The sampling method determined the sample size at 95% confidence level<sup>55</sup>. The raw population of each journal were sorted by decades, except for *Cancer Research*, where the papers since 1990 were sorted by every two years. This is due to the exceptionally large number of them. The groups sorted are considered as independent from each other. The sample size for each group was then determined and varies with the group size. Table 3.1 displays the scale of survey resulting from the sampling method.

**Table 3.1: Scale of survey**

<b>Journal title</b>	<b>Period of search</b>	<b>Raw population returned from search</b>	<b>Estimated population excluding estimated omissions (10%)</b>	<b>Sampled size including omission</b>	<b>Actual percentage of omission (%)</b>	<b>Sample size for analysis</b>
<b>JCB</b>	1962 – 2005	453	407.7	453	7.52	<b>419</b>
<b>PNAS</b>	1970 – 2005	1,191	1071.9	1,191	5.54	<b>1,125</b>
<b>Cell Death and Differentiation</b>	1972 – 2005	1,294	252	280	0	<b>280</b>
<b>Nature Cell Biology</b>	1999 – 2005 (established 1999)	58	52.2	58	6.9	<b>54</b>

<sup>55</sup> This step used probability proportional to size sampling method based on the following sources: Quinn and Keough, 2002; Sneath and Sokal, 1973; Sokal, 2012; WHO, 2015; and web version of software The Survey System.

<b>Nature Reviews Molecular Cell Biology</b>	2000 – 2005 (established 2000)	59	53.1	59	0	<b>59</b>
<b>Cancer Research</b>	1972 – 2005	3,313	1098.9	1,221	12.53	<b>1,068</b>
<b>Cell</b>	1987 – 2005 (archive available from 1987)	320	201.6	224	5.8	<b>211</b>
<b>FASEB</b>	1972 – 2005	802	302.4	336	11.9	<b>296</b>
<b>Total</b>	N/A	7490	3439.8	3822	N/A	<b>3512</b>

All papers sampled and screened were managed in spreadsheets. Five basic descriptions were used for filing, browsing, and retrieval: publish year, volume, issue, start page, end page. The next section will introduce my taxonomy of the diagrams, where more descriptions of category were used for paper retrieval. At the basic level, digital object identifier (doi) number was sometimes used, when page number is not available from the archive. A noteworthy example is the *FASEB Journal*. Section 4.2.8 will show that *FASEB* has a special category of articles since 2000. Articles in that category are first published online without page numbers before published in print with page numbers. The special category has resulted in some important patterns of visual communication in *FASEB*. In such a case, doi was used as an additional description in record management.

## 3.2 Quantitative analysis

The quantitative analysis is composed of categorisation and statistics of the visual items in papers surveyed. This method not only analysed the coverage of diagrams but also has taken qualitative rationale into account when categorising the diagrams. Different themes of diagrams are viewed as the embodiments of different research interests. For example, diagrams depicting entities have a different research focus from diagrams depicting experimental procedures. Thus they are categorised as different types and quantified separately. In this sense, the results can reflect the relative prevalence of different research focuses.

### 3.2.1 Number of visual items and diagrams

Numbers of visual items and diagrams in individual papers were counted. Technical papers in contemporary biological sciences have a nearly standardised way of ordering non-text items. Normally, non-text items are named “figures” and numbered in sequence. While some journals

number photographs and diagrams separately from data-intensive figures (such as curve charts and bar graphs), this study treats them all as visual items.

### 3.2.2 Categorisation of diagrams

The categorisation used in this study identifies five diagram types:

1. Object
2. Chemical structure
3. Experimental design
4. Mechanism
5. Other (miscellaneous)

Figure 3.12 presents the hierarchies of types and subtypes. This taxonomy was constructed based on my first-hand experience in biological practice<sup>56</sup>.

**Object:** The object type refers to diagrams depicting entities at any scale, from any aspect, and are composed of any visual elements. Given the diversity of object diagrams, this study used two axes—theme and visual element—to qualitatively identify several subtypes of the object diagrams.

Table 3.2 Subtypes of object diagrams and examples		
	Multiple visual elements	Two or single visual elements
Theme 1: Molecular levels	Receptor depicted with iconic parts, words, lines etc.	Protein sequence composed of letter abbreviations
Theme 2: Cellular level and above	Organisms composed of various iconic parts	Schematic drawing of cells in round shape

These two axes sub-categorised the object diagrams so that the prevalence of special themes can be quantified. Chapter Four will show that macromolecular structure, such as genetic substances and amino acids, is a dominant theme in this type. These structure diagrams typically contain fewer visual elements. The other common theme is depiction of biological entity, such as cells and tissues. These depictions are usually composed of various elements. Nonetheless, both themes contain exceptions.

Figure 3.1 presents two typical examples of the subtype that conveys molecular structure information and has fewer iconographic components. This subtype usually represents molecular structures by arranging certain letters in specific ways, where the letters are standardised

<sup>56</sup> Gross et al. (1990), Kemp (1997), Craver and Darden (2013). Near the completion of this thesis, I referred to Bechtel et al. (2014), Sheredos (2015), and Macleod and Nersassian (2015), ensuring both the originality of this taxonomy and its harmony with the existing literature.

abbreviations for names of the molecules or their parts (eg. DNA bases, amino acids). The arrangements represent the alignments. Examples in Figure 3.2 are typical forms of iconographic representation of molecular structures. In such forms, segments of the substances are normally illustrated with boxes, lines, and words. Arrows are sometimes used to indicate the length of the segments or the directions of biochemical reactions. Apart from molecular structures, cellular compartments (eg. organelles and receptors) are common themes of object diagrams and appear at slightly-lower frequencies. Figure 3.3 shows examples of these subtypes.

**Chemical structure** (abbreviated as **CS** in some of the figures in this thesis): This type contains diagrams dedicated to only representing structures of chemical compounds. Figure 3.4 provides examples of this type.

While this type can be considered in a broad sense as a subset of the object type, this study distinguishes it from the object type for two reasons. Firstly, these two types can be distinguished in terms of the standardisation of form. Diagrams of chemical structures have long-established and standardised sign systems, eg. representations of bonds and the abbreviations of chemical elements. This survey will show that object diagrams normally do not have standard sign systems. Apart from the aforementioned representations and abbreviations of macromolecules, object diagrams do not have truly standard elements. They have conventions, such as the ways to mark exons and introns in a schema of genome or the way to label proteins with their molecular mass. But the conventions vary in style and are not universal. They are usually embedded in non-standardised elements and arrangements.

The second reason to distinguish the CS type from the object type is the disciplinary distinction. This study focuses on reflecting the trends of visual communication in biology. To analyse the contents of biological diagrams, the object type that contains diagrams of biological materials must include DNA and proteins as well as cells and tissues. The non-biological chemicals, on the other hand, usually serve as experimental reagents. Chapter Four will show that the coverage of the CS type is very minor in cell biological journals (0-5% in proportion). *Cancer Research* has the only and especially high coverage of this type, for cancer studies tend to investigate lots of therapeutic chemicals.

To sum up the difference between the CS and object types, the object type in this thesis contains illustrations of compounds that *are* intervened in, whereas the CS type contains illustrations of chemicals that scientists *use to* intervene in biological mechanisms.

**Experimental design** (abbreviated as **ED**): Figure 3.5 and 3.6 present examples of this type. ED diagrams convey (1) experimental procedure, (2) procedural instruction of instrument, and (3) manipulation of experimental materials. The contents are varied, while performing a common function of illustrating the design of experiment. All these cases count as ED diagrams: an illustration of dividing a petri dish for different yeast cultures, a drawing of injection process of animal anaesthesia, and serial illustrations of gene targeting and recombination. In the original captions, scientists may use different yet clear terms to describe the themes of such diagrams, eg. “experimental design”, “experimental protocol”<sup>57</sup>, “procedures”, or “strategy”. The format and style of ED diagrams vary by the content, spanning from drawings of experimental settings (including biological and non-biological materials) to flow charts showing linear or non-linear procedures. Figure 3.5 presents a drawing of erythropoiesis (Figure 3.5A) and a scheme for genetic recombination (Figure 3.5B). Figure 3.6 shows an example of flow-chart style of representing concurrent steps.

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<sup>57</sup> It is interesting that, since the 1990s, the term “protocol” is increasingly used in the captions to refer to biological experiment procedures. This term suggests that the procedures are consented and widely accepted. Further study is needed to determine whether this term appears more frequently because of the trends since the 1990s or simply due to the increasing frequencies of diagrams (and thus the variety of language of the captions).

**Mechanism:** The mechanism type contains diagrams representing causal and explanatory models for physiochemical processes. Figure 3.7 to Figure 3.10 present some typical forms of mechanism diagrams. The contents and their aesthetics in fact vary greatly. The configuration can be either simple and linear or as complicated as a network. There are also cases of creative visual experiments which deviate from visual conventions.

This study uses these criteria for characterising mechanism diagrams:

- (1) In the author's own terms, their contents are described, categorised, or defined as “mechanisms”.
- (2) The ideas conveyed by these diagrams consist of *entities* (usually the acting units) and *activities*, where the entities and activities are configured to *explain* particular phenomena. Entities can be and are not limited to cells, chemicals, molecules, cell compartments etc. Activities can be and are not limited to stimulating, inhibiting, binding, signalling etc. Such decomposition is inspired by, yet not strictly following, the existing literature on biological mechanisms (Bechtel, 2006; Illari and Williamson, 2012)<sup>58</sup>. Given the variety of biological mechanisms, this study reduces the components to the minimum by not focusing on either the organisation or the function they may perform.
- (3) The visual arrangement of constituent entities and activities conveys *causalities* and *changes of state*.

**Other:** These are rare and miscellaneous cases, whose presence is up to 5% amongst all the five types in each journal through the period surveyed. Figure 3.11 shows two random examples of this highly-diverse type. This type does not meet any of the aforementioned criteria or share common subject matters<sup>59</sup>.

### 3.2.3 Frequency and proportion of diagram types

The coverage of different types of diagrams was calculated and compared in two aspects: proportion and frequency. The **proportion** of a diagram type was determined, for each individual journal, through dividing the number of the diagram type by the sum of all types. The results are the percentages of the diagram types in a journal of a period.

The **frequency** of a diagram type was determined, for each individual paper, through calculating the ratio of diagram to visual item. The number of diagrams (D) was divided by the total number of visual items (VI), producing a ratio D/VI. D/VI in general and D/VI of each diagram type were independently determined for each journal. The mean frequency of a journal was calculated for each decade: 1970s, 1980s, 1990s, and 2000–2005.

The results of the above calculations were processed with two kinds of software, Microsoft Excel<sup>®</sup> and SigmaPlot<sup>™</sup>, for statistics and graphing. Comparisons of the frequency and proportion were done longitudinally (through time) and horizontally (across types and journals).

<sup>58</sup> As mentioned above, my definition for “mechanism diagrams” is in harmony with Bechtel et al. (2014), and my definition for “diagrams” slightly differs from theirs due to my exclusion of data images. They refer to mechanism diagrams as a more restrict sense of diagrams (164).

<sup>59</sup> Some of diagrams in this type exhibit “branching” forms and a part of them belongs to phylogeny diagrams that are normally used in evolution studies. Pietsch's book (2012) on “tree diagrams” in biology details a dedicated volume of historical branching diagrams and appears to view branching diagrams as a special collection. However, my study categorises diagrams according to their subject matters but not styles. Those tree-like diagrams in my “other” type do not share common subject matters. They are defined as miscellaneous.

### 3. 3 Qualitative analysis

The qualitative analysis focused on the contents of the diagrams. This part closely examined the visual components and the configurations used to construct diagrams. Meanwhile, meanings and values embedded in both the components and the configurations were interpreted.

The initial plan was to employ automated techniques to interpret the contents of diagrams. This was intended to benefit from the development of algorithmic technologies for content-based image retrieval (CBIR) during the past twenty years<sup>60</sup>. However, recent computer science literature has emphasised the semantic gap between the ideal and realistic scenarios of image content recognition (Deserno et al., 2009; Wang et al., 2010). The current state of image-retrieval technology still greatly requires human judgement to achieve accuracy. Computer fails to recognise certain tacit characteristics of images that human perceives. Solutions to such challenges are still under development<sup>61</sup>. Thus no adequate automated technology of image analysis was available for the purpose of this study.

#### 3.3.1 Layers

The concept of dissecting diagrams according to their contents are borrowed from art history (Bender and Marrinan, 2010), as well as cultural geography and media communications (eg. Rose, 2012). The contents of diagrams are divided into three layers:

1. Visual element
2. Configuration (composition)
3. Style

**Visual element:** This includes all constituents that, in whatever forms, are present in the diagrams. Some visual elements are especially frequent in biological diagrams, such as basic geometric shapes (triangles, eclipses, squares, etc.), lines (solid and dotted), words, and arrows (in various forms). Scientists and artists sometimes create new forms of elements by arranging these existing ones. Thus the same elements in different arrangements may have different meanings in different contexts. For example, a circle can represent a gene in a diagram and a protein receptor in another. Some visual elements are specifically designed for exclusive representations. A commonplace example is icon of the mitochondria (Section 5.3.4 has a detailed discussion).

**Configuration:** This means the composition of diagrams and the arrangement of elements. It concerns not only the organisation of elements but also the ways to relate and separate them.

**Style:** This covers from the overall manner of composing the diagrams to the choice of elements in terms of aesthetics. For example, some diagrams follow visual conventions and mimic the appearances of special graphs (such as line chart). Some others tend to use extravagant elements.

Art history has extensive methods for studying the above three layers (eg. Barnet, 2003). Such methods allow the analysis of both aesthetics and materiality (eg. Bentkowska-Kafel et al., 2009). This study builds its qualitative framework partly through borrowing the methods from such literature<sup>62</sup>. Nevertheless, this study treats the diagrams as part of scientific argument rather than

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<sup>60</sup> Examples of early initiatives: Borowski et al., 2000; IEEE Workshop Proceedings, 1998; Niblack et al., 1993. Wang et al. (2010) reviews the development in digitally retrieving images via different ways.

<sup>61</sup> For example, Kumar et al. (2014) proposes a database approach that is not suitable for individual images analysis.

<sup>62</sup> Such as previously cited Bender and Marrinan, (2010) and Rose (2012).

artworks. Artistic aspects are considered coherently with their scientific meanings and their roles in scientific communication.

Meanwhile, this study does not examine the production value of diagrams, which is commonly discussed in art history literature. This methodological decision is based upon the fact that the diagrams surveyed are to be transferred digitally across a range of media to ensure the information conveyed to be disseminated in unchanged forms. Normally, the diagrams appear in electronic formats and then in print. Neither the features of the media nor the materials that compose the images can affect the quality of meaning conveyance. The value of communication through such digital images in bioscience journals is stable.

Interestingly, this *stability* results from the desire for *mobility*. Some sources have discussed the travelling of scientific knowledge across geographic and cultural distances<sup>63</sup>. This study treats biological diagrams as material vehicles for concepts. These vehicles need to be mobile to transcend the boundaries between various media used in different local settings. Their physicality is not necessary to the retaining and the disseminating of the information conveyed. Indeed, the artistic designs and aesthetic values of many diagrams were discussed in this study. But these features were considered in the context of “scientific communication via digital images”, where the production value of the original copy is not of interest. Also, there are cases of low-definition or even blurred images due to the state of technology at that time. Reading such cases can be challenging, but such a challenge was not taken into account in my discussion. In this study, aesthetics is considered in terms of effectiveness of conveying scientific ideas. There is no single standard for judging the aesthetic value of diagrams.

### 3.3.2 Criteria

The layers of diagrams as introduced in the previous section were dissected with five criteria.

**Appearance:** This includes and is not limited to size, shape, colour, special visual effect (eg. shadow, highlight, transparency, gradation), and font style of words (symbolic elements).

**Encoded meaning:** Elements and compositions in biological diagrams tend to have straightforward meanings. But some cases require decoding of both denotations and connotations. For example, as Chapter Four will show, some diagrams embed photographs imported from experimental images, where both the meanings and the signifying functions of the photographs are changed. In an example case, the denotation of the photograph refers to the observation of particular apoptotic events, and the connotation is the pathway to death.

**Sophistication:** Some elements are very basic and even primitive, while some others are complicated.

**Creativity:** This criterion concerns the use of traditional and relatively novel elements, compositions, and styles.

**Impact of technology:** Because the period surveyed has seen a considerable change of the state of technology, the impact of technological advancement on visual representation was discussed.

### 3.3.3 Contexts

The meanings of contexts of diagrams span a wide range. This thesis limited the range of contextualising the diagrams in four senses:

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<sup>63</sup> For example: Shapin (1998); Howlett and Morgan (2010).



1. Source of ideas
2. Perspective
3. Text
4. Scope of the discourse

This decision conformed to the information available from reading and interpreting the papers. Contexts beyond this direct sense, eg. the activities of diagram-making, were not considered.

**Source of ideas:** This refers to the source of meanings conveyed by the diagrams. For example, an icon representing a kind of protein may be a visual resemblance to the actual structure of the protein. Here, the process of protein structure determination is not explicitly represented in the diagram, yet influencing the design of the icon. Another example is the membranes of cell nuclei. In numerous diagrams, the membranes are represented by dotted lines, which represent the pores on the membranes. This characteristic of cell nuclear membranes was discovered decades ago, yet serving as the source of idea for designing this special visual element (dotted line). Thus this context is about the practice and the background knowledge embedded in the visualisation.

**Perspective:** As addressed in Section 2.1.1 and 2.5.1, this thesis does not use the term “perspective” in the traditional art history sense. This term refers to the angles and scales of investigating and understanding biological phenomena. For example, if a diagram is composed of a drawing of cell nucleus and letter abbreviations of DNA alignments inside the nucleus, it contains at least two perspectives: microscopic and molecular levels of interest. Section 2.4 has maintained that different perspectives for biological mechanism research can represent different fields of interest and sometimes different systems of practice.

**Text:** This study does not consider diagrams as necessarily supplemental or inferior to the text. Section 2.2 has maintained my position that visual representations in certain scientific practices function a lot more than aiding the text. The text surveyed in this study has two kinds. One is the original caption of the diagram, and the other is the body text of the paper.

In many biological diagrams, keys to the meanings of visual elements are provided by the captions. The informed viewer usually does not need the captions to interpret the meanings of diagram components, yet the captions may offer information about the author's reason for visually constructing their ideas in particular ways. In some rare, visually experimental cases, even the informed viewer may need the captions to understand both the meanings and the author's intention.

The body text includes methodology and experimental results of the papers. Taking it into consideration helps one contextualise the diagrams in the whole argument (the paper). It is commonplace that the components of diagrams are transformed and translated from either experimental design or experimental data. Considering the methodology and the results of the papers helps one appreciate such transformation and translation.

More importantly, the text can sometimes provide the details of how the author's perspective interacts with existing knowledge and other perspectives. Biological mechanism research must engage different perspectives (as reiterated through this thesis), and “puzzle-solving” is a popular phrase cell biologists use to describe the interactive approach to the explanations for biological phenomena<sup>64</sup>. The text may have the clue to the decisions made during the making of diagrams: why are some existing perspectives visually emphasised, and why are some visually black-boxed?

**Scope:** While this study focuses on a specific field, the scopes of both the journals and the papers

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<sup>64</sup> It is both hard to find out (and beyond the scope of this study) whether the use of “puzzle-solving” by biologists has received influence from Kuhn (1970, 35-42). It can be told from the papers surveyed that, though this use is consistent with Kuhn's sense, it usually emphasises more on the gradual, piecemeal process of building the whole scenario (mechanism) than the normality of practice.

are not homogeneous. The scopes vary in many senses, and the variety of the scopes affects the visualisation, as Chapter Four will show. For example, some of the journals surveyed are facing relatively esoteric groups, such as *Cell Death and Differentiation*, and some tend to engage a wider audience, such as *Nature Reviews Molecular Cell Biology*. Some of the journals concentrate primarily on theory, and some are data-oriented. Some of the papers are designed to quickly publicise the latest findings, while some emphasise both novel discoveries and previous achievements. Some of the papers concern specific, narrow topics, while some concern the bigger pictures that encompass related discoveries. Most of the times, such differences in scope are not explicit in the text but are embedded in the design and the editing of visual items (including data graphs).

### 3.4 Conclusion

This chapter has introduced my research object: diagrams in apoptosis papers retrieved from eight journals during 1972–2005. The previous sections have described the methods used to quantify the patterns of diagram coverage (number, frequency, proportion) and analyse the features of the contents, such as visual elements, composition, and style. The contexts of the diagrams are analysed in parallel to the features. The results produced through this methodology will be presented in Chapter Four.

## Chapter Four: Results

### 4.1 Introduction

This chapter presents the results from the survey. The overall goal of the survey is to draw the comprehensive patterns of visual communication in apoptosis research over a period of three to four decades. Rather than studying special individual images, this study seeks the trends over a large number and a long time frame. The methodology has been described in Chapter Three.

By design, this thesis makes a distinction between data and interpretation. The data is presented in this chapter, and Chapter Five will interpret it. Section 4.2 contains eight subsections, where each is dedicated to one journal. Volume II of this thesis contains all the figures numbered according to the sequence of their appearance in the text (Volume I). Because the data and the interpretation are closely tied to the figures, I suggest the reading of Chapter Four and Five to be always accompanied by Volume II.

The sections on individual journals organise the data as below:

1. Data profile.
2. Quantification: this includes proportion and frequency of diagrams both in general and of each special type.
3. Qualitative analysis: this analyses visual element, composition, and style of five diagram types. The contexts of diagrams (see Section 3.3.3 for definition) are discussed both in this chapter and Chapter Five.

In this chapter, biological concepts are explained as necessary. This is to analyse the meanings of the contents and contextualise them in the practice.

### 4.2 Results

#### 4.2.1 JCB

Figure 4.2.1.1 shows the scale of survey on *The Journal of Cell Biology* (JCB) and the omission in each decade from the 1960s to 2005. There is a surge of apoptosis papers in the 1990s. This observation is consistent with existing studies of the apoptosis field (eg. Garfield and Melino, 1997) and common expert opinions, reflecting the rapid growth and expansion of the field. Irrelevant papers are omitted at a rate less than 10% in average.

Figure 4.2.1.2 presents the ratios of diagram to visual item (abbreviated as D/VI hereafter and in Volume II) in each decade. The survey starts from 1972<sup>65</sup>, when apoptosis and related terminology first appeared in professional journals. A gradual growth of D/VI is clearly seen, suggesting a trend toward communicating with diagrams. Compared to other kinds of visual items, such as photographs and chart graphs, the D/VI is relatively limited (eg. in 2002, the ratio is around 8%). But this can be explained by the fact that the other visual items are experimental data, which must

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<sup>65</sup> Kerr et al. 1972.

be the major part of visual items in scientific papers. Some of the journals surveyed are quite high in D/VI, some are very low. Each journal has its own manner of employing visual means of communication. Figure 4.2.1.3 takes a closer look at the increase of D/VI from the 1990s to the 2000s, for these two decades witnessed a massive growth in apoptosis research. The increase of D/VI is nearly double and statistically significant.

Figure 4.2.1.4 compares the proportions of diagrams amongst types and between the 1990s and 2000s. There are two prevalent types: object and mechanism, which together take up 80% to 90% of the coverage of diagrams in both decades. The object type shows an increase in the 2000s, while the mechanism type remains the majority throughout. The other three minorities all decrease. This possibly results from the growth of object type and the unchanged proportion of mechanism type.

To explore the frequencies of these two major types, their D/VIs are compared in Figure 4.2.1.5. From the 1990s to the 2000s, both types significantly increase in frequency. The mechanism type exhibits a more radical increase than the object type. Such trends result in the even larger difference of frequency between these two types in the 2000s (Figure 4.2.1.6). Thus the mechanism type remains most prevalent in terms of both proportion (Figure 4.2.1.4) and frequency. In sum, diagrams are increasingly employed by the authors to convey ideas since the 1990s. This trend temporally resonates with the exponential growth of apoptosis field. Amongst the five diagram types, the mechanism type appears most frequently, with its frequency continually growing.

Here I start to present the qualitative results of the object type. In *JCB*, both the contents and the styles of object diagrams are varied. This feature is exemplified by Figure 4.2.1.7 to 4.2.1.11. Figure 4.2.1.7 presents an example of early (before 1990) object diagrams, which focus on depicting observations without adding much information that is not directly from observing. Apart from the added arrows and words, which symbolise the differentiation of cells, the main part of this diagram is composed of drawings of ultracellular visualisation. These drawings resemble the actual vision under the microscope. The viewer (even without much background knowledge) may recognise the effects of the transforming processes from microscopic photographs to diagrams, such as extraction of key information of the structure and degradation of irrelevant noise.

Figure 4.2.1.8 presents a 1995 case of similar characteristics, implying the continued use of traditional “resemblance” style of object type. While object diagrams in the 1990s became more diverse in style, traditional styles are not abandoned. But the developed technologies indeed show their influence on the changing aesthetics. The hand-drawing and irregular appearance of Figure 4.2.1.7 is different from the relatively well-ordered appearance of Figure 4.2.1.8. This difference might be just contingent due to the different appearances between the cells they depict (Figure 4.2.1.7: ciliary ganglia; Figure 4.2.1.8: intestinal epithelium). Nonetheless, it is plausible that both the graphic tools and aesthetics for producing object diagrams have changed during the nineteen years between these two diagrams. These two diagrams exemplify Lynch's (1990) process of making *transformative rendering* from photographs to diagrams (see Section 2.6 of this thesis). Their difference demonstrates a flexibility of such process. However, the following images in this and the other sections show that even the most straightforward type of object diagrams can exhibit sophistication that is beyond the scope of Lynch's thesis.

Figure 4.2.1.9 presents a special case of transforming a common style and content of object diagrams to a creative one. As mentioned in Chapter Three, schematic diagrams of macromolecular structures, eg. letter abbreviations of amino acids, are prevalent enough to be treated as a sub-type of the object type. As this chapter will show, since the late 1980s to the early 1990s, schematic diagrams of macromolecules drastically take over the coverage of the object type. *JCB* exemplifies such an increase of this sub-type, while being slightly later than other journals surveyed. Figure 4.2.1.9 illustrates the typical arrangement of amino acid sequence of an ion channel, but its

composition is neither linear nor boxed, as seen in countless examples of this kind. Instead, it combines the letter arrangement with a simplified depiction of the mitochondria membrane, where the latter serves as the background for illustrating the ion channel. In this background, a few words describe different loci, ie. cytosol and intermembrane space. This background offers space for arranging the letter abbreviations of amino acids according to their actual *topology* (Shimizu et al. 2001). The uniting of schematic structures and the background drawing contextualises the ion channel in its physiological environment. Object diagrams of structures tend to eliminate the contexts. This makes Figure 4.2.1.9 a special case.

Figure 4.2.1.10 shows a common style of representing macromolecules. This is a representation of different binding sites on a protein named ectactin. Since the 1990s, object diagrams increasingly tend to employ multiple simple elements to constitute complicated structures. A possible explanation is a temporal coincidence amongst three factors: (1) the growth of knowledge of macromolecular structures, (2) the development of graphic technologies, and (3) the wide spread of novel graphic technologies. This diagram is a typical example in terms of organising simple geometric shapes to compose a complicated structure. Later, this section will show that mechanism diagrams undergo a related visual evolution. Namely, the mechanism type—which is meant to synthesise other diagram types—increasingly incorporates such kind of object diagrams (ie. constituting complicated structures with simple geometric shapes).

Styles of object diagrams also evolve in parallel to the expansion of biological knowledge and the development of graphic tools. Such novel styles are either immature or not yet invented before this period. Illustrations of proteins are one of the most demonstrative case. Roughly since the mid-1990s, novel styles of protein diagrams appear more frequently. Ribbon diagrams and three-dimensional space-filling models are most common ones. However, Section 5.4.1 will explore that the novelty of these macromolecule diagrams cannot be solely attributed to the emergence of new digital tools. To the contrary, some of such “novel” styles have been cultivated in the hand-drawing era. They just did not proliferate in specialist communication until digital tools became popular. Section 5.4.1 will show that the relationship between ideas and technology is complicated in the case of evolution of macromolecule diagrams.

For other biological entities, there is also an increase in novel means of representing things that have long been known. For example, cell organelles are now imaged by novel experimental technologies and depicted with new graphic tools, even though they were discovered no later than the middle twentieth century. Figure 4.2.1.11 shows a set of mitochondria images. This image set is produced with electron tomography, which is a new imaging technology of reconstructing micro-level structure through obtaining and collecting cross-sectional images from electron microscopy. The original paper is published in 2000, only two to three years after the launch of this technology (Ahsen et al. 2000). Such a quick adoption of novel means of both exploring and representing biological structures confers new appearances on long-known objects. Scientific approach and visual representation are changed at once by this adoption.

The experimental design (ED) type of diagrams remains in low proportion throughout the period surveyed, while containing various styles. The most common styles include linear arrangement and flow chart. The former describes simple, sequential procedures, and the latter arranges basically-linear yet concurrent or branching processes. Such primitive styles normally employ simple visual elements, eg. words, arrows, and basic geometric shapes. Experimental devices are sometimes drawn in a figurative way.

There are also rare cases in this type, whose visual elements seem barely functional. Figure 4.2.1.12 shows two ED diagrams from the same paper. The key messages (ie. two different actions of injecting reagents into the mice) are represented by black and red symbols. Given that the key

messages are conveyed clearly, the detailed drawings of the mice and the syringes appear to be extravagant. The drawings provide a pictorial feature and perhaps add aesthetic value, but they do not facilitate the conveyance of ideas to a significant extent. These images are not technical instructions for injection but cartoon representations. The viewer does not need the drawn mice and syringes to understand how to do injections into the mammary gland and the tail vein. The implication of such cases (which are relatively few) is that the author's attention is occasionally paid to details that tend to be ornamental rather than technically important. As the following sections will show, non-scientific visual trials appear in all diagram types in all the journals surveyed. Perhaps sometimes visual experiments are not about facilitating technical communication but reducing the possible dullness of highly-dense visual language.

Figure 4.2.1.13 and 4.2.1.14 show two examples of another minor type, the “other” (miscellaneous) type. The styles of this type in *JCB* are as mixed and various as their functions. Figure 4.2.1.13 combines the time course of experiment with observed consequences, making itself a half-way visualisation between experimental design and mechanism types. The experimental results are *almost* explained by the process (represented by words) above the time axis, while the direct causality is missing. Missing of causal relationships makes this process a mere mixture of experimental procedures and cell events. The other processes beneath the time axis are chronologically-listed observations. The sequential arrangement of descriptive words does not explain the underlying mechanic process. This part of the diagram functions more to display the experimental results than to convey a mechanistic model. Nor is it a genuine display of experimental results, for it lacks data.

Figure 4.2.1.14 has obvious visual differences from Figure 4.2.1.13 for having a composition resembling a chart graph. It too has a time axis and chronologically-listed observations as Figure 4.2.1.13 does, while it contains no scale and number on either of its axes. The chart-graph composition clearly conveys the relationships between the observations, ie. the upward and downward curves that represent expression of different genes. No quantification is provided. It is plausible that the relative arrangements of the curves are not directly associated with the actual data. This is a truly *schematic* representation. The original caption of this diagram actually says that the purpose is to “schematically depict” (Estus et al. 1994) the hypothesis of necessary increase and decrease of genes in apoptotic situation. This diagram is an example of borrowing existing, well-established forms of visual language yet using them in a somewhat modified form. Normally, the modification involves only removal of actual values. The results from the other journals will show that charts and bar graphs are common forms to be adopted for such schematic depicting.

The mechanism type in *JCB* exhibits a tendency to evolve through the decades in terms of: (1) complexity of visual elements, (2) complexity of component perspectives, and (3) creative compositions that is more capable of embracing the former two trends. Along with the creation of new styles and elements, long-used styles and elements are not abandoned. It is the uniting of traditional and novel ways of representing mechanisms that enriches available iconographic resources for accommodating the exploding ideas.

Figure 4.2.1.15, 16, and 17 present examples of relatively primitive forms of mechanism diagrams. Figure 4.2.1.15 is the earliest one (1988), containing just basic elements: geometric shapes (circles and triangles), simple graphs (lines and arrows), words, a specifically designed icon, and a metaphorical sign from non-expert area. The special icon is the antibody sign (the fork-shaped sign), a widely-accepted visual convention of representing antibody (or antigen receptor) in biological disciplines. The metaphorical sign is the death cross, which is borrowed from everyday context to convey the concept of “death” of the cell (but not of the individual, as it usually represents in everyday context). The key message is simple: thymocytes in the thymus differentiate

into cells that either express CD<sup>4</sup> and CD<sup>8</sup> antigens or lack one of it. The former kind has low level of T cell antigen receptor (the antibody sign), and the latter kind expresses high level of the receptor. The former will then commit apoptosis. The narrative in this diagram is nearly linear, with only a branching point in the middle. This diagram exemplifies the features of early mechanism diagrams: basic elements and fewer dimensions. In other words, mechanistic models in the early years of apoptosis research appear to involve one or few viewpoints that can be exhausted with basic elements arranged in simple compositions.

The cases in Figure 4.2.1.16 are demonstrative of this manner. Both images are from the middle to late 1990s and contain only symbols (including question mark) and arrows, except that Figure 4.2.1.16B has two squares that “box” the two groups of cell events. This “boxing” serves no role in communicating the core technical information but visually separates the two groups. Both images are structurally similar to flow charts. Their narratives are both composed of linear processes and a few branching points. These two 1990s diagrams possess not much novel feature compared to Figure 4.2.1.15, which is published nearly ten years earlier. This shows that traditional ways of composing visual language remain useful in the time when novel features emerged.

Figure 4.2.1.17 exemplifies the proliferation of ideas and perspectives in mechanism diagrams since the middle 1990s. It demonstrates an intermediate status of mechanism diagrams evolving. The composition and the elements are basic, while the perspectives embedded are multiple and complex. This 1996 diagram uses entirely the same visual elements as Figure 4.2.1.16, while systematically translating the processes by adding extra perspectives. The words in the rectangle represent the intentional periodisation of cell events from removal of NGF (nerve growth factor) to apoptosis. Although this diagram also uses a time axis for sequential events, it does more than merely listing the events like Figure 4.2.1.13 does. It categorises the observations into increased phenomena (labelled by upward arrows) and decreased ones (labelled by downward arrows). The causes of all these events are indicated by words arranged on the top of the diagram, displaying the cause-effect relationships that are necessary to mechanisms. This diagram contains a higher level of perspective that *explains* the phenomena than the other components. This feature contrasts Figure 4.2.1.17 to its contemporaries (Figure 4.2.1.16).

Figure 4.2.1.18 is another example of the intermediate status of evolution. It demonstrates another feature of the evolution of mechanism diagrams, namely the enrichment of visual elements. The mitochondria icons have two different forms: one represents an intact and healthy status, and the other represents a collapsing and apoptotic status. These are cartoons of mitochondria produced in the way of Lynch's “transformative rendering” (1990, 160). The structure of mitochondria is unlikely a novel idea in the mid-1990s, but such vivid cartoon representations rarely appear earlier. The embedding of such cartoons in mechanism diagrams also seems novel. The advancement and spread of graphic technologies in the middle 1990s might explain an emergent trend to visualise existing ideas in novel ways. The embedding of a table in this diagram is also creative. The contents of the table are actually the key to the meanings of the small simple signs, eg. red and green triangles. This table certainly facilitates the process of looking up the meanings. The key message of this diagram is straightforward: some apoptosis-related proteins distribute differently in different statues during the apoptotic process, where Bcl-XL protein has an inhibition effect on this process. Such a message has an inherently pictorial feature and is hard to efficiently convey by propositional means. This diagram shows how efficiently a diagram conveys information about mechanisms.

The complexity of visual elements grows to accommodate complex perspectives. Figure 4.2.1.19 to 4.2.1.22 present examples of a relatively mature status of visual evolution. Figure 4.2.1.19 is a 2002 diagram containing multiple visual elements that are not seen in earlier cases. The most noteworthy point is its composition, namely a parallel display of two fates of the cell: proliferation (left) and

apoptosis (right). These two fates have similar forms and elements. This implies the author's confidence in clearly conveying their distinction. Using the same cell background for two opposite mechanisms does not confuse the viewer, for the viewer intuitively considers the blank space between the two scenarios as a separation. This is an imaginative and abstract boundary, which acts in Bender and Marrinan's sense (2010) to "correlate" different images so that the whole image is read in a coherent manner (2010, 71). This blank space separates the two scenarios, so the viewer understands that they are not simultaneous events happening within the same cell, despite the same background. Such parallel display of different pathways and the use of blank space as *both* separation and correlation are common in the diagrams surveyed.

Figure 4.2.1.20 also arranges two comparable scenarios in parallel, but the large overlap of their component entities and processes makes it necessary to entirely separate these two scenarios. This 2004 diagram is reflective of the enrichment of visual elements. Just like the mitochondria icons in Figure 4.2.1.18, both the mitochondria and the endoplasmic reticulum (ER) icons here are new resources for representing long-existing ideas. The visual similarities between such icons and the entities under the microscope exemplifies the biological convention of transforming photograph to diagram via simplification and modification. Nonetheless, such new icons transformed from traditional vision have not appeared frequently until recent decades. They became common in mechanism diagrams roughly at the same time with the sophistication of visual elements. In this sense, sophistication of visual elements in the 1990s seems to be driven by new graphic tools. But two visual elements in this diagram adds an extra point that new tool is not the only driving force. One element is the icon of perforins proteins from CTL (cytotoxic T lymphocyte), the other is the depiction of pores on the membrane of target cell. These are visual elements that could not have been designed until the knowledge about the action of perforin (pore-forming protein) is established. In sum, the growing multiplicity of visual elements reflects the rapid development of digital graphic technologies, while it seems actually due to the growing complexity of ideas.

Figure 4.2.1.21 and 4.2.1.22 both contain complicated icons composed of basic geometric shapes, as seen in Figure 4.2.1.10. Instead of inventing new icons, this is a way of creating visual elements from new perspectives. In *JCB*, the rapidly expanding knowledge of molecular structures tends to be represented by an increasing use of this kind of new elements. Possible explanations include: (1) the invention of entirely new elements is less convenient than arranging traditional ones to construct new appearances, and (2) the newly-explored structures are normally too complicated for schematisation. For example, a highly schematic depiction of a global protein barely differs from a simple sphere. But this global structure can be depicted more vividly through arranging some spheres to resemble the three-dimensional structure, as seen in a space-filling model. Comparing these two diagrams, Figure 4.2.1.21 is more obvious in rearranging traditional elements, and Figure 4.2.1.22 pays much attention to artistic effects.

Figure 4.2.1.22 is more recent (2002) and benefits from advanced graphic technologies, such as three-dimensional graphic effects. The component activities in this model are better narrated by iconographic resources than words: the formation of laminin surface (the blue plain), and the recruiting and anchorage of laminin-1 molecules (the serial blue dots). The key message is about a *dynamics* composed of space and time. Its multi-dimensionality is more suitable for diagrammatic than verbal descriptions. Those graphic effects do not add much (if any) technical meaning, but they decorate the narratives in a way that aids the viewer's animation of the dynamics: the changes of spatial arrangement of the entities through time.

The above cases demonstrate the evolution of mechanism diagrams from a general aspect. There are also rare cases in the mechanism type in *JCB*. Figure 4.2.1.23 to 4.2.1.25 present three special cases. Figure 4.2.1.23 contains serial cartoons of the cleavage of two kinds of protein subunits. Dynein is a protein responsible for mobility of microtubule (a cell skeleton) via binding to it with



mediation of its subunit *dynein intermediate chains* (CD-IC) and a subunit of dynactin, *p150<sup>glued</sup>*. Cleavage of CD-IC and *p150<sup>glued</sup>* results firstly in the loss of microtubule mobility and secondly in apoptosis. This diagram uses arrows to indicate the direction of dynein “walking” along microtubule in normal status<sup>66</sup> (shown by the upper cartoon). In the lower cartoon of apoptotic status, an icon of scissors cuts the two protein subunits. This cutting leads to an interruption of dynein's walking, as represented by a cross sign. Such employment of everyday metaphorical sign (the scissors) is also seen in Figure 4.2.1.15, where a death cross represents apoptosis. In all the journals surveyed, metaphorical icons borrowed from non-specialist areas appear in mechanism diagrams, but at low frequencies compared to other basic icons. Scissors are commonly used to represent protein cleavage in terms of their everyday meaning of “cutting”.

The most special feature of this diagram is not about the scissors but the depiction of motion. The heading directions of the protein subunits shift after the cutting, rendering an animated effect of the story. This diagram borrows a conventional comic way of representing motion to show: (1) in the upper cartoon, the continuing walk of dynein; (2) in the lower cartoon, the consequence of interrupting the walk. These conventions visualise the inertia of motion. This vivid depiction of the effect of the inertia animates the process of protein cleavage, through an entirely metaphorical way. A viewer with background knowledge about cell mobility does not really expect the actual dynein cleavage to be like this scene. The animation has no technical meaning, but it makes the reading process more intuitive. Section 5.3.2 will discuss such cases of using non-specialist elements in conveying professional ideas.

Both the visual elements and the composition of Figure 4.2.1.24 are somewhat basic, but this diagram is creative because of the way it joins two scenarios of cell cycle together. Circles are usually used to represent the cell cycle due to its analogy to repetitive and cycling process. The two cycles here can be viewed as two stages of cell events: the large circle stands for a cell cycle continually leading to proliferation, and the small circle stands for a reversible status of quiescence. The large circle is divided into certain phases labelled by different symbols, such as S for synthesis phase and M for mitosis phase. The small circle contains only one phase, ie. a temporary suspension of cell proliferation and differentiation. The circular composition of this quiescence status represents its reversible nature. In the presence of high level growth factor (GF), a regulator gene *Myc* activates the following: the cycle of proliferation status, cell differentiation, and apoptosis. A tumour marker *carcinoembryonic antigen* (CEA) inhibits the above effects of *Myc* through turning the cell into quiescent status. Thus the joining point of the two “stages” is the turning point of cell fate from death to survival. Here, a “CEA” symbol and an arrow together indicate the entry to the “survival” sphere. The creativity of this diagram lies in this joining point of two cycles. It concisely conveys the shift between the two fates.

Diagrams with “network” composition are very rare in *JCB*. Figure 4.2.1.25 provides an example. Note that the rarity of such network diagrams does not necessarily imply that network theory is less concerned in cell biology at the time surveyed. To the contrary, the analysis of network diagrams has four implications:

- (1) an emergent concern about biological networks since the middle 1990s;
- (2) the introduction of mathematical modelling into cell biology to solve molecular interaction problems;
- (3) a growing trend to systematically consider biological reactions;

<sup>66</sup> Technically, this “walking” process is called *minus end-directed transport* because dynein moves toward the minus end of microtubule. But the term “walk” is also used a lot in expert communications.

- (4) importantly, the sophistication of mechanism diagrams that matches the scientific need to represent complex systems.

In Figure 4.2.1.25, four boxed groups of proteins are categorised according to either their species or the systems they mainly act within. Experimental data is used to model the structured information about a complex system of interactions amongst all these proteins and the mitochondria. As the original paper suggests, the lack of existing experimental approach to systematising heterogeneous and distributed knowledge of apoptosis promotes the introduction of mathematical modelling into the apoptosis field. The consequence of the exponential expansion of apoptosis field since the early 1990s is a huge and heterogeneous body of knowledge. In this sense, modelling is introduced into apoptosis just like it is introduced into other fields of fast-proliferating and heterogeneous knowledge. Diagrams function better than words in representing the modelled complexity. When graphic technologies are developed parallel to the growth of both structure biology and apoptosis field, this development contingently renders diagrams the best candidates for visualising complex pictures of apoptotic protein interactions.

#### 4.2.2 PNAS

Figure 4.2.2.1 shows the data profile of *PNAS*. Between 1970 and 1989, only three papers are returned by archive search, and no paper is omitted. The surge of apoptosis papers since the 1990s is consistent with the observation of *JCB*, as well as the other journals surveyed. The proportions of omitted papers are 4.55% in the 1990s and 6.29% in the 2000s. All relevant papers are sampled.

D/VIs are shown in Figure 4.2.2.2. The results start from 1990 due to an absence of diagram before 1990. The D/VI decreases from 0.078 to 0.082 between 1990 and 2005, but such a small difference is barely meaningful. Thus the D/VIs in *PNAS* remain quite steady through 15 years. Figure 4.2.2.3 shows the proportions of five diagram types in two decades. There are two notably prevalent types: object and mechanism. But it is only in the 1990s that the object type has taken up over 50% of all diagrams. After that, the object type decreases alongside the increase of proportion of the mechanism type. Interestingly, in the 2000s, the experimental design (ED) type becomes more than twice than the 1990s, while the other two minorities remain unchanged.

The frequencies of the two prevalent types are shown in Figure 4.2.2.4. Neither type shows a statistical significance between the 1990s and 2000s. As the frequency of the object type decreases, the mechanism type increases. The overall pattern is a pair of inverse changes. This implies that the object type becomes less needed and the mechanism type is increasingly used. The increase of ED type should be considered, too. Through two decades, the frequency of this type increases from 0.006 to 0.013, exhibiting a more drastic change of frequency than the mechanism type. Possible explanations include the following: (1) an increase of special experimental procedures that are better conveyed via visual means; (2) a stronger tendency of the authors to represent experimental design with diagrams.

From this paragraph onwards, the qualitative results are presented. I start with the object type. The majority of object diagrams in *PNAS* are about macromolecular structures. This is the same with *JCB* and will be seen in the other journals surveyed. The forms vary from letter abbreviations to schematic depictions (eg. pictures of relative spatial arrangements of protein domains), and then to more sophisticated forms such as ribbons and three-dimensional space-filling models. In the case of protein representation, these contents are sometimes integrated to display multiple levels of a structure. Figure 4.2.2.5 is an example of integrating the information of amino acid sequences

(upper part) and the depictions of tertiary structures (lower part). Generally, in the journals surveyed, such integration of different aspects of protein representation has not appeared until the middle 1990s. Again the same with *JCB*, not until recent decades have sophisticated protein representations appeared frequently in *PNAS*, despite that some of them (eg. ribbon diagrams) had been developed before the spreading of digital technologies. Figure 4.2.2.6B also presents a ribbon diagram in the 2000s. This finding will be interpreted in Section 5.4.1.

Figure 4.2.2.6A provides an example of more visually special way to convey protein information. Figure 4.2.2.6A is a “helical wheel” diagram, a special kind of protein representation that offers an overview of the positioning of amino acids (represented by plots) in the secondary structure of protein (ie.  $\alpha$ -helix, one of two kinds of protein secondary structure). Through using different colours of the plots, the spatial relationships between hydrophilic and hydrophobic amino acids can be recognised easily without referring to the detail of amino acids. In this diagram, hydrophobic amino acids are blue, and hydrophilic ones are red. The yellow plots are neutral amino acids. Thus it is visually straightforward that one side of this helix is hydrophobic (lipophilic) and the other side is hydrophilic. This helix is the C-terminal domain of a pro-apoptotic protein Bim. Containing such a terminal means the amphipathic nature of Bim and its potential to bind protein (hydrophilic) to membrane (lipophilic). As intriguing as the case of ribbon diagrams, helical wheel diagrams have been developed in the late 1960s<sup>67</sup>, yet this kind remains very rare in all journals surveyed apart from this 2004 example. This can be a coincidence, if the papers sampled do not concern much about protein properties that are better represented with helical wheels. But it is also possible that the emergence of computer software for generating helical wheels—some of the generators can be freely accessed on the internet—has contributed to the spread of this kind.

Figure 4.2.2.7 is a special case of object diagrams in terms of its synthetic feature. The ribbon representations have a background context, which is depicted with basic graphs. This background represents the boundary sites between two different membranes. The message of this diagram is to show how the protein residues form ion permeation pathways (channels) across these membranes. The structures of the formed channels are the key information and a professional concept, while the background information is basic knowledge of cell biology. Thus the sources of information are heterogeneous. So are the visual representations of them. This synthesis of specific and basic concepts contextualises the structures in their loci of functioning. Synthesis of heterogeneous ideas is a common feature of mechanism diagrams, while it is less common in object diagrams than mechanism diagrams. Figure 4.2.2.7 shows that synthetic features are not exclusive to mechanism diagrams.

The synthesis of heterogeneous information in Figure 4.2.2.8 is a different kind. It joints histological photographs with drawings, directing a reading pattern of inter-referencing between the data and the diagram. This synthesis exemplifies a relatively traditional way of producing diagrams: transformative rendering from photographs to diagrams (Lynch, 1990, 157-62). Meanwhile, it also shows that the relationship between photographs and drawings is more than one-way transformation. The diagram *adds* information, such as vessels and other tissues in the dermis layer, which comes from existing knowledge and serves as the background information. Apart from the simplification of photographs, there is not much visual similarity between the drawing and the photographs, but their joint arrangement and the addition of indicative elements (words and lines) both facilitate the inter-reference between them. In following sections, more cases from the mechanism type will exemplify such an inter-referencing pattern of reading between data images and drawings. I will also show that the uniting of data images and drawings in mechanism diagrams tends to require complicated means of inter-referencing. Then Section 5.5.3 will interpret these inter-referencing patterns.

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67 Schiffer et al. 1967.

Parallel to the dominance of macromolecular structures in the object type, the majority of the experimental design (ED) type is about genetic recombination. This remains unchanged when the frequency of this type increases twice from 1990 to 2005. Given the rapid growth of biotechnology in the 1990s, it is arguable that the fast-expanding apoptosis field increasingly deploys genetic technologies to investigate the molecular details of mechanisms. That is, the pattern of visual culture in specialist communication reflects the pattern of practice. The diagrams of genetic manipulations have quite similar styles, and Figure 4.2.2.9 presents some typical examples. Figure 4.2.2.9A represents genetic substances in a linear way, and Figure 4.2.2.9B represents with rings. Conventionally, ring diagrams are used in the case of using bacteria for recombination, for a circular DNA (bacterial plasmid) is used as targeting vector. While these diagrams reflect the emergent focus on macromolecule manipulation in the 1990s, it is worth investigating why diagrammatic representations are increasingly inescapable—when the ideas conveyed by these diagrams actually could be expressed by words.

A minor part of the ED type is about drawings of experimental settings and organisms, normally with arrows indicating the directions of processes. Figure 4.2.2.10 is a special example of having no arrow, ie. no suggestion of the sequence. At first glance, it appears as an object diagram, a drawing of petri dish for microorganism or yeast seeding and growing. However, this is not an object diagram but a display of the design for growing four different strains or same strain under four different treatments or mutations. This is indicated by two visual elements: the crossed lines dividing the dish into four areas and the labelling words. The adjacent experimental photograph displays the results of yeast growth. This ED diagram also invites an inter-referencing reading pattern (similar to Figure 4.2.2.8) between the data image and the drawing, which visually resemble each other. The drawing and the photograph complement each other as the start-point and the end-point of the experimental process—the diagram describes the *plan* for action, and the photograph displays the *consequence* of action. The difference between Figure 4.2.2.8 and 4.2.2.10 shows the variety of cross-referencing reading pattern.

Figure 4.2.2.11 uses basic graphs to represent the experimental process of inducing cell death in a specific brain area. But the simplicity of the elements does not make it easily comprehensible to a reader without background knowledge. The basic structure of this diagram represents a circuit in the basal ganglia, which is a brain region (or a gathering of nuclei) crucial in a range of physiological functions. Voluntary movements are one of these functions, where this paper concerns the pathology of voluntary movement function, ie. Parkinson's disease. The circuit runs between two parts of the basal ganglia, striatum (Str) and substantia nigra (SN). Striatum projects axons into the part pars compacta in substantia nigra (SNpc), and SNpc in turn projects back to striatum. Such mutual projections result in mutual “signal sending”, namely communication via neurotransmitters, between these two areas. To depict the circuit accurately, this diagram employs a standard sign, ie. the grey line with a dot at one end and a splitting at the other. In neuroscience, this conventional sign specifically means a neuron (the dot) projecting its axon (the splitting) to a target and sending signals to it. The use of standard sign makes this diagram visually compact and straightforward, though only to the informed viewer. The other components in this diagram are also simple: a cross at the striatum area and the “QA” symbol above it mean the destruction of striatum with injection of quinolinic acid (QA). Because of the standardised visual language of neural circuit, it is easy to understand that such a process is to induce programmed cell death (apoptosis, PCD) in substantia nigra. Two ideas are effectively conveyed: (1) the apoptosis in substantia nigra (represented by the “PCD” symbol) and (2) the positive results (represented by plus signs). In sum, this diagram conveys an experimental model and the outcome, neither of which is complicated. The background of this diagram is actually a part of basal ganglia circuit diagrams that are visually familiar to neuroscientists. Potential confusion may occur to non-experts due to the use of visual convention in neuroscience and the abbreviations of anatomical regions. Therefore, a paradox takes place: it is the

adoption of simple, standardised signs and abbreviations that makes the message intuitively discernible to the informed viewer, while raising a barrier to outsiders.

The chemical structure (CS) type and “other” type are both rare in *PNAS*. The CS diagrams are all about reagents used in experiments. The “other” type is even rarer. In *PNAS*, this type includes diagrams different in their functions but same in the lack of causal ideas. Usually, they display research results, eg. pedigree tree diagrams that classify experimental results. The compositions and styles are varied. Apart from the branching form of pedigrees, there are diagrams that have chart-like arrangements (yet presenting no scale and number). There are also Venn diagrams. Venn diagrams are used to show the overlapping components between different groups of observations.

Figure 4.2.2.12 is an example of the “other” type. The original paper studies the target proteins via proteomic technology (Aulak et al. 2001). Those proteins can be nitrated in the body, resulting in pathological conditions. This diagram classifies and displays the activities and events the nitrated proteins are involved in.

Figure 4.2.2.13 is another example of the “other” type and more visually complicated. This network diagram shows the biological relationships amongst a group of genes. Each node represents a gene and is outlined by a geometric shape. Different shapes mean different functional classes. The lines connecting these genes represent different biological activities, eg. inhibition and transcription. Each line is labelled with a letter symbol, which is the abbreviation of the activity (such as A for activation). The key to symbols on the right side describes the meanings of the visual elements. In all *PNAS* papers sampled, only two network diagrams are found. Figure 4.2.2.13 is from 2005, and the other (not shown) is from 1996. Such a limited number of cases makes it unlikely to discuss whether or not the rapid growth of systems biology since the mid-1990s is associated with the emergence of network diagrams on macromolecules. Nonetheless, the years of appearance of such network diagrams in *PNAS* and the other journals surveyed may leave a clue to future comprehensive study on network diagrams.

Figure 4.2.2.14 presents two examples of mechanism diagrams before the mid-1990s. Both have relatively simple compositions and basic visual elements. Figure 4.2.2.14A has three parallel lines representing three different progressive events in T cell activation, where the general background (T cell activation) is represented by the words on the top. The top line represents two kinds of gene action, which occur in sequence and have effects on cell cycle progression. Part of the cell cycle is represented by the middle line, where the abbreviations (letters) represent different stages of the cycle. The bottom line represents the action of Bcl-2 protein that is correlated with the cell cycle via action of a cytokine, interleukin-2 (IL-2). Only the middle line is composed of two arrows, suggesting a directional process. The other two lines stand for actions involved in different stages of the process ending at particular points. This diagram, though simple in both composition and element, unites at least three packets of information from three perspectives: physiological cell cycle, molecular gene actions, and signal transduction within cytoplasm carried out by signal-sending molecules (such as Bcl-2 and IL-2). Additionally, this diagram adds a perspective for the inter-relationship between the three perspectives. This diagram exemplifies two common features of mechanism diagrams: synthesis of different perspectives and addition of extra-perspectives. Section 5.5 will detailed these two features.

Figure 4.2.2.14B has a simpler composition compared to Figure 4.2.2.14A, but it also synthesises different perspectives. The key message is that exposure to some factors and nutrients prevents apoptosis. These “good things” are simply represented by the descriptive words outside the cell icon. The “smiley” of the cell metaphorically represents the status of living and suggests the goodness of those stimuli. This straightforward composition unites different packets of information and contains causality (ie. those good stimuli cause survival) in a subtle way due to its simplicity.

This diagram appears as a typical case of early mechanism diagrams, which tend to contain less-complex information and simple causal relationships.

The two mechanism diagrams in Figure 4.2.2.15 employ exactly the same visual elements: words, basic geometric shapes, and arrows. Both are in black and white and published in the mid-1990s. Yet the meanings of these elements in these two diagrams are quite different. This demonstrates the versatility of basic elements. In Figure 4.2.2.15A, the two squares are used to outline cellular events, whereas the squares in 4.2.2.15B work together with the eclipses to identify the existence of protein molecules (such as Bcl-2 and Bax). Thus their functions are different: the geometric shapes in 4.2.2.15A mark the ranges of phenomena, and the geometric shapes in 4.2.2.15B represent the physicality and the ontology of entities. The squares in 4.2.2.15A have only one layer of function: outlining and separating two groups of events. The choice of the shape does not necessarily help this meaning. The squares could even be removed, for the reader can tell from the splitting arrows the distinction between two groups.

The squares in 4.2.2.15B have another layer of meaning: visual analogy. Each of them is coupled with either a same or different partner. The meaning of this coupling is dimerisation of proteins—coupling of identical elements means the existence of a homodimer, and coupling of different elements means a heterodimer. Thus the coupling arrangement of these elements (and their word labels) is to visually analogue the coupling of proteins. Meanwhile, the overall composition of the coupled elements does not mean anything physical. The positioning of the element couples merely serves to conveniently gather all the hypothetical interactions (represented by paired reverse arrows). In sum, these elements represent the entities in an abstract and imaginative context. This is a typical way of composing mechanism diagrams in recent bioscience. New (and sometimes complicated) icons are created to resemble the appearances of novel entities, while the compositions do not resemble the actual environments. Yet sometimes, the compositions of mechanism diagrams resemble the cellular space via transforming microscopic pictures. When there is a conflict between the clarity of conveying ideas and the aesthetics of visual resemblance, visual resemblance tends to be sacrificed to clarity. Figure 4.2.2.15B shows such prioritisation.

A comparison between Figure 4.2.2.16, 4.2.2.17 and 4.2.2.18 suggests that the visual language in apoptosis research might have responded to the rapid growth of novel ideas in a delayed manner. Figure 4.2.2.16 is from 1996, and the latter two are published in 2005. Their temporal deference is not consistent with their difference in complexity of information. The 1996 diagram actually exhibits a higher level of complexity, as it not only integrates more kinds of entities and events but also contains a sequential classification of these components. On the right side, there are four stages of apoptosis progress<sup>68</sup>. This classification adds a perspective that does not belong to the components of the cell model, making the content of this diagram more complex. Section 5.5.4 will explore such “supra-perspectives”. Meanwhile, the meanings of the visual elements are plural to the extent that the reader needs to carefully refer to the word symbols. The arrows, while having similar (if not the same) shapes, have impressively plural meanings<sup>69</sup>. Moreover, the original caption clarifies that the arrows “do not necessarily indicate direct interactions”<sup>70</sup>. This implies an exclusion of some interactions and requires the reader to identify the meanings more carefully. The contrast between the highly simplified visual elements and the complexity of perspectives shows the shortage of visual language. The implication here is a possible gap between the exponential growth of apoptosis field and the evolution of diagrams.

The messages of Figure 4.2.2.17 and 4.2.2.18 are less complex, but their visual elements possess

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68 The final stage “post mortem” is somehow confusing, for this is not the condition after a cell's complete death. But it is obvious that the added axis is to show the causal and temporal relationships between the four stages.

69 See the caption and text of the original paper: Vaux and Strasser, 1996.

70 Vaux, and Strasser, 1996, Figure 1.

higher sophistication than Figure 4.2.2.16. In these two cases, the use of graphic technologies catches up with both the increased complexity of ideas and a growing emphasis on the aesthetics. There are still plural meanings of visual elements in Figure 4.2.2.17. For example, arrows in the same form respectively represent causation (in the lower part, caspase-9 leads to apoptosis) and relocation (in the upper part, there is a JNK-dependent phosphorylation of c-Jun). The description of abstract ideas quite relies on words. But there is also a differentiation of arrow meanings. Three sets of arrows indicate different actions: positive activation or causation, inhibition, and negative feedback loop. Such a differentiation of meanings, while being somewhat rough, renders the arrow meanings more intuitively readable than Figure 4.2.2.16. The meanings of the signs are less ambiguous, too. Molecules and cell organelles have their own icons in specific colours and shapes. Some of the icons resemble the appearances of the entities, eg. cell membrane and mitochondria. The other icons, ie. the proteins, do not exhibit visual similarity to the entities, while their forms follow certain visual conventions in biology.

Figure 4.2.2.18 is another case containing specifically designed icons and exhibiting intuitive readability. By multiplying the forms of visual elements, this diagram draws distinctions between different sets of entities (eg. molecules on the inner mitochondrial membrane and Bax channel) and between different kinds of concepts (location, activities, etc.). In the lower part, it provides the key to the meanings of icons, making the reading process more convenient. The plural meanings of the words are comparable to Figure 4.2.2.17 but much less ambiguous than Figure 4.2.2.16. The words indicate either locations (eg. cytosol) or activities (eg. lipid peroxidation). In sum, in the two 2005 diagrams (Figure 4.2.2.17 and 4.2.2.18), the visual elements differentiate to accommodate plural ideas. The differences between the 1996 diagram (Figure 4.2.2.16) and these two suggest an evolution of visual language toward the capability of accommodating complex ideas.

Figure 4.2.2.19, a 2002 diagram, demonstrates both the multiplicity of perspectives (as seen in Figure 4.2.2.16) and differentiation of visual elements (as seen in Figure 4.2.2.17 and 4.2.2.18). The axis on the right side indicating sequential processes is similar to the axis in Figure 4.2.2.16. The separation between transcriptional induction and transcriptional repression by using the symbols on the top adds another descriptive axis. The three membranes partition the space into four layers, namely from external environment of the cell to the space within the inner membrane of mitochondria. These loci of cell events are as rich as combining the information taken from Figure 4.2.2.17 and 4.2.2.18, while the meanings of the visual elements exhibit a modest degree of plurality. In other words, the plurality of meanings of the visual elements is less than Figure 4.2.2.16 and higher than Figure 4.2.2.17 and 4.2.2.18. It may be a coincidence that this diagram is published (2002) between them (1996 and 2005). If this is not purely coincidental, the implication is very suggestive of the existence of an intermediate status of visual evolution.

Rarities appear in both the 1990s and the 2000s. But the 2000s have more odd examples. Rarities are cases that appear at very low frequencies and do not have typical styles. Figure 4.2.2.20 to 4.2.2.24 provide some examples.

The 2004 diagram presented in Figure 4.2.2.20 is a case of introducing data images into the configuration of mechanism diagrams. Figure 4.2.2.8 and 4.2.2.10 already presented similar cases. Unlike those two object diagrams, the employment of two data images (histological photographs) in Figure 4.2.2.20 changes the function of them. The two histological photographs on the right side are to represent cell differentiation and apoptosis respectively. However, in laboratory practice, which is their original context, they are more like the indicators of but not the icons for cell differentiation and apoptosis. In this mechanism diagram, these two photographs are in small-to-middle size (compared to the other visual elements). The visual emphasis is not upon them. The other visual elements are produced by graphic tools and not quite resembling the actual entities. Interestingly, the addition of these two photographs is not necessary to the narrative of the mechanism. The

function of the photographs appears to be “standing for” the two final destinies of the cell. Unlike the previous integrations of data images and drawings, Figure 4.2.2.20 does not require much inter-reference or comparison between the photographs and the other part of the diagram. Replacing the two photographs with words or other signs would not alter the meaning. The use of the two histological photographs appears as iconic and not irreplaceable. The original meaning of the photographs is converted from indicating the phenomena to representing the phenomena in an iconic way (see Section 5.2 for the definitions of different signs in this thesis).

Figure 4.2.2.21 and 4.2.2.22 are examples of object-centred mechanism diagrams. This kind tends to contain one or more object(s) especially large in size and depicted in detail. In Figure 4.2.2.21, both diagrams focus on membrane receptors: 4.2.2.21A is about platelet-derived growth factor (PDGF) receptor, and 4.2.2.21B is about tumour necrosis factor (TNF) receptor. These two diagrams coincidentally use quite similar icons to compose the receptors, where the remaining parts contain only arrows and words. The compositions of the receptors are simple but at the same time detailed enough to display the fundamental arrangements of the functional domains of the receptors. The contrast in size and detail between the receptors and the remaining parts clearly indicates the centrality of the receptors in the overall mechanisms.

Figure 4.2.2.22 is a different case of object-centred mechanism diagrams. While the “main characters” in this diagram are also proteins, they are not illustrated by schematic drawings. The icons symbolising the proteins are the ribbon diagrams of the structures. The other elements are basic. The overall composition is also straightforward and has a linear backbone. The key message simply includes (a) activation of protein Grx2, (b) the activating and inhibiting factors, and (c) the consequences of Grx2 activation. The symbols and the circular arrows on the “activated” (right) side mean that Grx2 takes electrons from the two reductases and that the electron-uptake leads to reductive reactions. The similarity between this diagram and the previous object-centred cases lies in the visual contrast between the most important entities and the other components. Moreover, some visual elements in Figure 4.2.2.22 not only are basic but also have a style that aesthetically contradicts the sophisticated ribbons.

Figure 4.2.2.23 exemplifies modular integration of one diagram type into another type so that a new meaning of the synthesis emerges. Figure 4.2.2.23A is an independent ED diagram that illustrates the process of transfecting two kinds of fusion proteins at once (ie. cotransfection) in a cell. The two proteins (DBD and VP16) then bind to an enzyme  $\beta$ -gal. This complex then binds to the site GAL4 on chromosome, forming a transcription control complex that has effects on CD4 antigen expression. Apparently, such a process is better communicated via visual means than words. In the same paper, two mechanism diagrams (Figure 4.2.2.23B and 4.2.2.23C) convey the apoptotic effects of the above experimental manipulation. In 4.2.2.23B, some of the visual elements imported from 4.2.2.23A are combined with new—yet not very different—icons to form a structurally-similar big icon complex. This complex means replacing the previous fusion proteins with two others for a new experiment. Causal arrows and descriptive words are added next to this icon of complex to convey the apoptotic mechanism. In 4.2.2.23C, the same elements are again used to represent a similar protein complex, which has different fusion proteins and is for another new experiment.

I refer to the feature that connects these three diagrams as a *modular* use of visual elements. The core structure of the drawing of the protein complex repeatedly appears in several diagrams throughout the paper, where both the themes and the details vary with different practices. The core structure is either imposed new elements (in 4.2.2.23B and 4.2.2.23C) or rotated (in 4.2.2.23C), while its basic form and meaning remain stable. In other words, the core structure serves as a *module* that is subject to relocation, rotation, and slightly morphological change, so it fits into different contexts of use. Section 5.3.1 will discuss how such module-like role of visual elements may contribute to a temporary visual consistency that facilitates the conveyance of ideas.



Compared to the creative modular use of visual elements, Figure 4.2.2.24A presents a truly rare case that appears to be too creative to communicate effectively. This is a 2004 diagram of general apoptosis mechanisms that involve well-known genes and proteins in this field. The symbols located centrally show that the key message of this diagram is apoptosis mechanisms induced by sphingosine (Sph). The composition has a cycle style because Sph-induced apoptosis is defined by the author as a “vicious cycle” (Suzuki et al. 2004): the higher the Sph level is, the more likely the cell undergoes apoptosis. The depiction of interactions between those well-known apoptotic molecules, such as caspase-3 and Bcl-2, is based on existing knowledge. Only the sphingosine-involving part, mainly on the left side, represents the original finding.

Temporally quite close to this diagram, Figure 4.2.2.24B shows a diagram from the fifth edition of a widely-used textbook *Molecular Cell Biology*. It contains almost the same entities and activities, while having a typical style of biological mechanism diagrams. Its composition is obviously distinct from the circular structure of 4.2.2.24A. The key difference between their components is that 4.2.2.24B does not concern the apoptotic effect of sphingosine. Instead, it shows how the absence of trophic factor results in cell death and that the presence of trophic factor helps the cell survive. No cycle is involved here. Thus no circular visualisation is needed for narrating the mechanism. The composition is easy to understand. It is arguable that this easiness is not an outcome of the use of multiple visual elements but of the relatively conventional arrangement. Comparing Figure 4.2.2.24A with 4.2.2.24B demonstrates how radically biological mechanism diagrams can vary in style due to the messages they need to convey. In 4.2.2.24A, none of the visual elements is beyond visual convention. However, the viewer's eye needs to wander about with the aid of the text until it finds out how to follow this exceptionally creative composition.

### 4.2.3 Cell Death and Differentiation

140 apoptosis papers are sampled from 647 search results (Figure 4.2.3.1). From 1996 (which is the year of the journal's establishment) to 2005, the D/VI increases from 0.111895 to 0.1773 without statistical significance (Figure 4.2.3.2). The proportions of different diagram types in 1996–1999 and 2000–2005 are compared. This comparison (Figure 4.2.3.3) shows that the proportion of mechanism type decreases relatively, while the other four types increase. However, the mechanism type remains major, despite its decreased proportion from 73% to 50%. The object type increases most and has a rate of increase at about 62%. The other types do not show obvious growth. The “other” type includes only phylogeny diagrams, which are not seen in the previous sections, and the actual number is only three.

The frequencies of two prevalent types (object and mechanism) in the two periods are compared (Figure 4.2.3.4). Both types show an increase in frequency. This is consistent with the overall increase of diagrams. But the increase has no statistical significance. This might be due to the limited number and the large variance of the samples. It should be noted that, since the journal was established in the late 1990s, the overall period surveyed spans no more than a decade.

Here I start presenting the qualitative results. Just like *JCB* and *PNAS*, the majority of object diagrams in *Cell Death and Differentiation* are about representations of macromolecular structures, which include (1) schematic drawings and (2) letter abbreviations representing the structures of genome and protein (or amino acids). Rarely, there are morphological diagrams. For example, Figure 4.2.3.5 (2001) illustrates the distribution of cell substances at different stages of nuclear events. Figure 4.2.3.6 (2005) displays the structure of a nuclear membrane channel. The

improvement of graphic technologies since the mid-to-late 1990s has some impact on the visuality. The drawings of objects tend to be more colourful and sometimes sophisticated in style than those in the 1990s. Nonetheless, not much difference between the two periods is found in terms of the contents and the compositions. This may be explained by the late foundation of this journal in 1996, when advancements in graphic technology already had influences in both everyday life and professional areas. Meanwhile, although new technologies show influence on the colouration, the object diagrams through the period surveyed still employ relatively traditional ways of composing the visual elements.

The number of chemical structure diagrams is very low (only two, but both include various compounds in combined images. See Figure 4.2.3.10 for examples). Both cases appear in the 2000s and contain representations of synthesised and commercially available compounds. In this journal, the use of artificial chemicals is usually about treating the cells for experimental intervention. The chemicals are functional drugs, which are either apoptosis-inducing, eg. artificial retinoid in Figure 3.2.3.10.A, or anti-apoptotic (survival-promoting), eg. artificial peptides in Figure 3.2.3.10.B.

The experimental design type does not exhibit much difference between the two periods in terms of visual element, composition, and style. The styles tend to be as simple as linear representations (Figure 4.2.3.7 and 4.2.3.8) or chart graphs (Figure 4.2.3.9). Such simple, non-novel styles are seen in the other journals surveyed. The impact of novel graphic technologies, while notable in the object type, is not obvious in this type.

The mechanism diagrams in *Cell Death and Differentiation* have no unique style compared to the other journals surveyed. Their ways of composing temporal and spatial information are not beyond some typical configurations that are seen in many papers and textbooks. This is shown by comparing the four diagrams from Figure 4.2.3.11 to Figure 4.2.3.14. The visual elements have various forms, which range from relatively basic kinds (such as words, basic shapes, and arrows in Figure 4.2.3.12), to novel kinds, such as slightly complicated icons that represent the structures of cell components (see the “proteasome” and the “FADD” receptor in Figure 4.2.3.13). The improvement of graphic technologies has an impact on some cases. For example, the colour gradation, irregular shapes, and three-dimensional reflections and shadows belong to such cases in Figure 4.2.3.14. These effects are made by new graphic tools. On the other hand, as seen in *JCB*, the growth of knowledge seems to have led to creation of new icons. The proteasome in Figure 4.2.3.13 is represented by a schematic icon resembling the actual structure. Such resemblance might not have been possible until the discovery of crystal structure of proteasome in the late 1990s (eg. Voges et al., 1999). However, all such evolutions of visual elements do not parallel an obvious evolution of their configurations. The arrangement of old and new elements follows traditional ways of representing cell mechanisms.

With regard to traditional configurations of mechanism diagrams, I add two interesting points. Firstly, the mitochondria appear to be visually emphasised in diagrams with simple styles and elements. While the visual elements are basic and the diagrams are usually in black and white, the mitochondria are the only entities that have specifically designed icons. Such icons resemble the ultrastructure of mitochondria with different degrees of schematization. Figure 4.2.3.11 is an example. This observation is not universal. For example, Figure 4.2.3.12 does not have a specifically designed icon for the mitochondria. But this observation is widely seen across the journals surveyed and will be discussed in Section 5.3.4.

Secondly, everyday visual elements are sometimes imported to the visual language of professional diagrams. As the following sections will show, such import is relatively low in frequency and probably correlated with the advancements of graphic tools. But it still happens across the journals surveyed, suggesting a common attempt to introduce non-specialist elements into expert visual

language. For example, the scissors in Figure 4.2.3.14 mean “cleaving” or “cutting”. The insertion of an icon of scissors into the caspase-3 enzymatic pathway represents the cleavage of cellular and nuclear substrates by caspase-3. In everyday context, icons of scissors are used in a range of commodities. For example, an icon of scissors (normally accompanied by a dotted line) on a food package means “cut here”. In such a context, one understands the meaning at first glance without much need of verbal description. Section 5.3.2 shall discuss, in parallel with Gooding's case (1990) of developing visual language in physics, the use of non-specialist visual *vocabulary* in developing biological visual language.

The “other” type contains three cases. Its proportion remains quite low (Figure 4.2.3.3: 0% in the 1990s and 5% in the 2000s). The three diagrams have similar “branching” configurations. Such forms are usually considered as phylogeny diagrams. Phylogeny diagrams originated from evolutionary biology. In cell and molecular biology, phylogeny is an effective way to display the relations amongst molecules that share a common origin and branch out as associated families or subfamilies. Figure 4.2.3.15 is from a paper studying the structurally homologous relationships between apoptotic proteins of human and bacteria. It shows a family of human apoptotic proteins and their prokaryotic homologies. Figure 4.2.3.16 is from a review paper on apoptotic protein database. It displays a group of proteins, in human and other species, that contain a common subunit (the element in the central). Both diagrams are representations of the systematic view for specific entities. As mentioned in Section 4.2.1, systematic studies of molecules began proliferating in the mid-1990s. The launch of this journal synchronised with such a trend, and the journal does contain representative cases.

#### 4.2.4 Nature Cell Biology

The two *Nature* journals surveyed in this thesis are both founded around 2000 and have low numbers of search results: *Nature Cell Biology* is founded in 1999 and has 58 apoptosis articles; *Nature Reviews Molecular Cell Biology* is founded in 2000 and has 59 apoptosis articles (for the latter see Section 4.2.5). In *Nature Cell Biology*, 4 results were omitted (3 erratum statements and 1 editorial, Figure 4.2.4.1). 93% of all was analysed. These articles are in five categories: communications, “News and Views”, letters to the editor, research papers, and reviews. The “reviews” category is not at all prevalent. Thus the relatively high D/VI (0.24, see Figure 4.2.4.2) does not result from the review papers, which are the kind of paper that heavily use diagrams. This high D/VI is noteworthy, for it is twice of the previous journals: *JCB* has an average D/VI of 0.08, and *PNAS* has 0.09. Meanwhile, this D/VI is still distinguishable from the exceptionally high D/VI seen in journals mainly composed of review papers, such as *Nature Reviews MCB* (0.85).

Object and mechanism diagrams are again the two prevalent types in terms of proportion (Figure 4.2.4.3). There is no chemical structure diagram. This seems to result from a feature of this journal that only key information to the novel findings is visualised. Limit of article size does not seem to have an effect here. The average page number is 6.25, which is not statistically different from, and even less than, the average page number in *PNAS* (5.93). In fact, a comparison between the four journals so far shows that *PNAS* may have an obvious tendency to restrict the article size (Figure 4.2.4.4). Both the *Nature* journals have higher average page numbers than *PNAS*. The absence of chemical structure diagrams might be due to other reasons, such as the scope of this journal.

The mechanism type is the most prevalent type throughout the years surveyed. To ensure that the inclusion of 1999 does not affect the result significantly, the proportions of diagram types in the

period 2000–2005 was separately calculated. The proportions of diagram types in 2000–2005 are almost the same with the period 1999–2005. the ED type is still quite minor, as seen in the other journals. All the cases in this type are about genetic recombination. The CS type remains absent.

The D/VIs of the two prevalent types show the special prevalence of mechanism diagrams (Figure 4.2.4.5). While its proportion is just twice as the object type, its massive presence within the visual items is significant. Its D/VI (0.20) is lower than *Nature Reviews MCB*, where the D/VI of mechanism diagrams is dominantly high (0.75). But again, because this journal contains several kinds of papers other than reviews, the high frequency of mechanism diagrams may reflect an emphasis upon mechanisms in non-review articles.

The contents of the two prevalent types do not have uniform styles, while they do in *Nature Reviews*. The majority of object diagrams are about macromolecular structures (Figure 4.2.4.6). This is very similar to the previous journals. These diagrams of macromolecular structures are typically simple in configuration, such as letter abbreviations representing the sequences. Only one case is not about macromolecular structure: Figure 4.2.4.7 is an illustration of a cell membrane receptor. It has a neat configuration that is comparable to the uniform style of diagrams in *Nature Reviews* (see Section 4.2.5). The font style is also very similar, if not the same.

Similar to the object type, the mechanism diagrams in this journal generally do not contain anomalous elements beyond certain conventions. They focus on the most relevant information, without distracting the viewer with radically creative elements and styles. Figure 4.2.4.8 contains two examples of mechanism diagrams that employ visual conventions, though they exhibit different degrees of complexity. Their visual elements are mostly basic and simple. The cell membrane in Figure 4.2.4.8B looks slightly complicated, but it is just a schematic delineation of the lipid bilayer. Their similarity in both element and style may be due to either a coincidence of using the same graphic tool or the culture of this journal.

The two diagrams in Figure 4.2.4.9 have some artistically creative features. They both represent the collapse of the mitochondria (which is a critical event in apoptotic progress) and depict the normal and apoptotic statuses of the mitochondria. It is not scientifically necessary to separately depict the two statuses. Many mechanism diagrams of apoptosis only have mitochondria icons in normal, integral shapes and do not mislead the viewer to an interpretation of healthy conditions. Thus the value of separating the two statues is aesthetic. It also makes the interpretation more intuitive. Such cases of aesthetic consideration are found in mechanism diagrams across the journals studied. The vivid cartoon-like styles of these two diagrams also facilitates the interpretation.

Metaphorical and analogical signs are used in some cases. The seesaw between life and death in Figure 4.2.4.10 and the death cross in Figure 4.2.4.11 serve as examples. In the visual culture of cell biology, seesaw and death cross are both very common. A cross metaphorically represents cell death. A seesaw icon is an analogy to the balance between a pair of opposing conditions, eg. survival and apoptosis, inflammation (activation or hyper-activation of immune system) and immune suppression. The seesaw analogy is sometimes put visual and sometimes verbal. Here I demonstrate this common use of seesaw analogy with two examples from journals not surveyed by this thesis. Figure 4.2.4.12 is from a paper in journal *Nature Medicine* and studies the immune response in sepsis. The seesaw analogy does not appear in the visual form but in the paper title (“*The Sepsis Seesaw*”), referring to the healthy balance (homeostasis) between inflammation and immune suppression. Yet this chart-style diagram has another metaphorical sign, the skull that represents death. Similar visualisation of death has been seen in the previous section, while the “death” here is the death of an individual but not the cell. Figure 4.2.4.13 is from journal *Cell Host and Microbe*, where three small diagrams of seesaws represent three stages of tuberculosis induced by mycobacterial infection. The visualised “balance” between pro- and anti-inflammatory

conditions means a controlled condition, in which bacterial proliferation is restricted. Section 5.3.2 will discuss the employment of metaphor and analogy in biological diagrams. I will discuss how these non-specialist elements play roles in both developing professional visual vocabulary and reasoning about mechanisms.

Comparing the five diagrams from Figure 4.2.4.8 to 4.2.4.12 can reveal a subtle yet noteworthy consistency in their styles. As mentioned, this journal has no uniform style for mechanism diagrams, where *Nature Reviews MCB* has (see the next section). But these five diagrams have some components in common: the font styles, the arrows, the shapes of icons, and the ways that the icons are coloured, highlighted and shaded. Their styles are, in some senses, not entirely distinguishable from one another and from the diagrams in *Nature Reviews*. If this consistency in the diagrams of Nature Publishing Group journals is not coincidental, it can be assumed that some aesthetic consideration and artistic modification are part of the standard process for publishing.

#### 4.2.5 Nature Reviews Molecular Cell Biology

This journal was established in October 2000 and has a relatively small number of papers, where 59 articles focus on apoptosis. The scope of this journal centres on reviews that aim to help cell biologists “constantly communicate with” their neighbours (Mitchell et al., 2000, 1) in a wider community. Therefore, articles in this journal focus more on the overviews of significant developments than the details of practice.

In the 59 apoptosis papers, 38 short articles contain no scientific diagram (Figure 4.2.5.1), and very few of them have data graphs. The majority of this population have photographs that only serve a decorative function. Figure 4.2.5.2 is a typical example of such decoration. Because the title is “Molecular Assembly Line”, this photograph of a mobile car assembly line shows this metaphor. Articles containing only such decorative images are not review papers and belong to the category “Research Highlights”. This decorative feature actually serves the aim of this special section. The first issue of this journal maintains that this category is “a bright and dynamic section that brings to life some of the most exciting research papers from the past month or so”<sup>71</sup>. The decorative images can serve this purpose via making certain abstract ideas more discernible.

4 papers were omitted from the remaining population of apoptosis papers for having no figure at all. 17 papers were sampled and analysed. The D/VI is impressively high (0.85) compared to the other journals surveyed. In terms of proportion, the mechanism type is the most major type (Figure 4.2.5.3). The object type follows by an obvious margin (48%). The other three types are either rarely present or absent. Given the very high D/VI as a background, the frequency of each type is calculated as the ratio of “type to diagram” rather than “type to visual item” (the latter applies to the other journals). Figure 4.2.5.4 shows the significant ( $p < 0.0001$ ) prevalence of mechanism diagrams.

This journal has a uniform style for diagrams, which is recognisable at a quick glance. This uniformity is seen in the colouration, the shapes of elements, the forms of icons, and the font style of words etc. I start exploring this uniformity with the object diagrams. Figure 4.2.5.5 presents four diagrams that have two points in common: (1) they illustrate different kinds of proteins, (2) they all focus on protein structures (ribbons and molecular complexes). While these diagrams are from two different authors, they are visually so similar that they appear to be produced under particular

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<sup>71</sup> Ibid.

standards. Figure 4.2.5.6 provides a comparison between two object diagrams from two different authors. Without any overlapping between the kinds of protein they represent respectively, these two diagrams exhibit surprising similarities (if not a uniformity) in their style. A good example is the way they represent CARD domain. CARD (caspase activation and recruitment domain) is a kind of protein motifs that appears widely in various proteins. Both diagrams in Figure 4.2.5.6 contain CARDS, but the CARDS are embedded in different proteins. CARDS in these two diagrams are coloured differently (A: medium pink; B: light purple) and in different shapes. Despite such different details, these two images still “look similar”. Actually, they use the same colours and shapes in different ways to represent different units of the objects.

This is why the uniform style is impressive—the repeated colours, icons and configurations have different meanings in new contexts. That is, the continuity of artistic design and the discontinuity of meanings act together to distinguish different messages, while the aesthetics across different diagrams remains consistent. The anatomy of the brain in Figure 4.2.5.7 again demonstrates this uniformity of style. While depicting an object that has nothing related to the previous cases, this diagram repeats their colours, the line style, and the font style.

Another general feature of the object diagrams is the absence of letter abbreviation representations of macromolecular structures, which are prevalently present in the other journals. The diagrams of macromolecules (eg. proteins) in this journal tend to be about the three-dimensional structures. The simplest style of them is schematic representation of protein subunits (eg. Figure 4.2.5.6). This may be due to either the editor's decision or the limit of article length, or both. Nonetheless, as Section 4.2.4 and Figure 4.2.4.4 have shown, the page numbers in the two *Nature* journals are about average to high. Thus the absence of diagram of basic structures is plausibly a result of the editor's decision, instead of the limit of article length. This review journal is more inclined to condense the visual messages. Background information (such as letter abbreviations) tends to be omitted. This selective and condense way is effective in communicating the most important findings.

Figure 4.2.5.8 exemplifies an integration of different perspectives for investigating an object (the mitochondria). Again, the uniform style is recognisable from the font style, the lines, and the colouring etc. But the key point of this case is about inter-referencing between data images and drawings, which is a special pattern of reading and has been seen in some previous cases. Unlike typical object diagrams, this diagram does not concern a particular structure but the processes of mitochondrial fusion and fission. Such an implicit dynamics makes it nearly a mechanism diagram, but it still lacks causality. The composition of this diagram is a uniting of experimental photographs (the time-lapse confocal microscopic pictures in the upper panel) and schematic illustrations (the cross-sections of mitochondria during fusion in lower left and fission in lower right). The illustrations are more than renderings from simplifying and transforming the photographs, for they add biochemical information that is not accessible through the microscope. These two illustrations not only complement each other with “actual” and “schematic” aspects but also act together to offer different visions of the objects at different scales and from different angles. The time-lapse photographs bridge the two static illustrations of statuses by providing an animation of the passage of time. Meanwhile, the two cross-section illustrations provide molecular descriptions for the events that are photographed. The added biochemical information is about the key molecules of the coupling processes (eg. mitofusin and GTPs). Via inter-referencing between different parts of the illustrations and the photographs, the statuses of the entities can be understood from both morphological and molecular aspects.

The uniform style is impressive in the mechanism type. Figure 4.2.5.9 presents two mechanism diagrams from different papers and authors. The two mechanisms have some molecules and pathways in common. Just like the object type, the consistency of aesthetics coexists with a flexibility of details. The same subunits in these two different mechanisms are represented by

different elements. The overlapping molecules (eg. cytochrome c and pro-caspase-9) and pathways (eg. the formation of apoptosome by pro-caspase-9, Apaf-1 and cytochrome c) are depicted with different shapes and colours. But the overall style is the same and consistent with the other papers in this journal. There is also a repeated use of particular elements. The graphs representing the cell membrane and the mitochondria are obviously from the same graphic database. The arrows and the font style, as well as the pattern of the background colour gradient, are the same in these two diagrams. Perhaps such a coexistence of uniformity and flexibility is how this journal maintains its visual coherence while not confusing different visual narratives with one another. The uniformity highlights a special aesthetics of this journal, while not affecting the effectiveness of communication.

Figure 4.2.5.10 provides more examples of how this journal produces recognisably stylish diagrams with its own rules. These rules are especially noticeable in mechanism diagrams because of the multiplicity and heterogeneity of the visual elements. Again, these two mechanism diagrams are from different papers and authors. The mitochondria, the arrows and the font style still repeat what have been seen in the previous cases. So do the colours and the pattern of colour gradient. Some new elements are added, eg. the skull that symbolises death and the apoptosome structure that is visually more complicated, but the design of these added elements follow the uniform style.

Contrast to the addition of elements in Figure 4.2.5.10, the two mechanism diagrams in Figure 4.2.5.11 reduce some elements. It only employs lines, arrows, and words to represent the dynamic processes, with an exception for the complicated mitochondria icon in Figure 4.2.5.11B. Note that this is the same mitochondria icon that appears in the two diagrams in Figure 4.2.5.10. This icon can be viewed as a template, and the use of template icons suggests manipulation of diagrams by the journal for visual consistency. While the elements and the configurations are both relatively basic compared to the previous cases, the background colour gradient, the words, and the arrow style reinforce the uniform style.

To sum the qualitative findings, the aesthetic style of diagrams in this journal is highly consistent. The style is seen in the repeated use of particular elements and similar compositions. The repeated elements are imposed different meanings in different contexts, so the relationships amongst the same elements are rebuilt in every new context. This makes the diagrams as wholes new narratives.

#### 4.2.6 Cancer Research

Compared to the other journals surveyed, *Cancer Research* has a very large population of apoptosis papers (Figure 4.2.6.1). There are at least two possible explanations. Firstly, the total number of papers in this journal is very large. Secondly, apoptosis is central to cancer research, for cell survival is closely correlated with carcinogenesis. The field of cancer research focuses heavily upon potential therapeutics that may induce cancer cell death *in vitro* and/or *in vivo*. A considerable number of cancer research papers focus only on single apoptotic pathways. Complex scenarios of cell mechanisms tend to be less concerned. The search results from this journal are reflective of such a tendency.

Given the large population, the sampling is conducted with a finer interval (2 years) than the other journals (10 years) (Figure 4.2.6.1). Due to the limitation of the online searching device of this journal, the search for the two keywords (“apoptosis”; “cell death”) was carried out separately. Figure 4.2.6.2 shows the two groups of results. The “cell death” group has more papers omitted than the “apoptosis” group. This is because it was sampled after the “apoptosis” group and that the

duplicates have been removed earlier.

The D/VIs remain very stable from the 1990s to the 2000s (Figure 4.2.6.3). In the 1990s, it is 0.039, and in the 2000s it is 0.041. Both sample sets have quite small variations within the group. It is noteworthy that *Cancer Research* has a very low D/VI compared to the other journals. Figure 4.2.6.4 presents a comparison between the five journals surveyed so far, where *Cancer Research* has the lowest and the most stable D/VIs. *JCB* has a low ratio in the 1990s. However, as shown previously, the coverage of diagrams in *JCB* grows in the 2000s. *PNAS* also has relatively stable D/VIs, though still much higher than *Cancer Research*. It is also shown in this figure that the two *Nature* journals have the largest coverage of diagrams. Figure 4.2.6.5 further shows that the D/VIs in *Cancer Research* are stable through four decades. It appears to be lower in the 1970s, but this may just be due to the very small number of papers in the 1970-1980s. No statistical difference is found between these two periods.

The proportions of diagram types in *Cancer Research* vary by period. The change in the distribution of diagram types is impressive (Figure 4.2.6.6 and 4.2.6.7). Amongst all the five types, only the mechanism type shows a distinct pattern of growth. It gradually increases from 25% to 46% in forty years, but it has never exceeded 50%. The other types have fluctuated up and down, showing no regular tendency to either increase or decrease. Apart from the object type in the 1970s, there is no dominant type in any period. Also, the seemingly dominant proportion of the object type in the 1970s is not meaningful, for the total number is very small (only 4) and that this period only has three types (Figure 4.2.6.6). The comparison of the numbers between the five types (Figure 4.2.6.8) also shows an obvious re-distribution of different types through the decades surveyed. This comparison shows that only the mechanism type has a pattern of proportion growth. But this is not directly shown in the numbers of diagrams—as mechanism diagrams increase a lot, both object and chemical structure diagrams also exhibit a large increase since the 1990s.

The frequencies of different diagram types (Figure 4.2.6.9 to 4.2.6.12) fluctuate respectively through the decades surveyed, too. Again, the only exception is the gradual growth of the mechanism type. The experimental design (ED) type has a surge in the 1980s, but the actual number of this type at that time is not larger than the others (Figure 4.2.6.8). Actually, the ED type is the most stable one in terms of number. The presence of the object type appears as relatively significant in this period. But this is only because the other types evenly divide the remaining coverage of diagrams.

The overall trend of the visual culture in this journal has three points. Firstly, the culture is very data-oriented, intensively focusing on data images. Secondly, the coverage of diagrams in general is thus very low, but it remains stable without being gradually suppressed. Thirdly, through the period surveyed, mechanism diagrams are increasingly used, yet the scopes for representing mechanisms are normally narrow and about therapeutics-related pathways. These three observations can be explained by the nature of the field of cancer research. Cancer studies are highly pragmatical in terms of their purpose to fight the disease. It is a long way to go from bench study to bedside application, so frontier discoveries are expected to be released as soon as possible. This journal has a special and large category of articles named *Advances in Brief*. Papers in this category are shorter than typical research papers, containing only data graphs and no diagram. Due to the large number of these *Advances* papers, the overall pattern of visual items in *Cancer Research* is much data-heavier than the other journals surveyed. Given such a background, the growth of the mechanism type is especially noteworthy. This growth implies that, even within such a data-oriented visual culture and a narrow scope for single pathways, the authors still increasingly pay attention to visualising mechanistic explanations.

Here I start presenting the qualitative results. Similar to the previous journals, the majority of object



diagrams in *Cancer Research* concern macromolecular structures. The representations still include letter abbreviations, schematic drawings, and ribbon diagrams. Early object diagrams tend to depict experimental instruments without conveying the design of procedures. Thus they are not categorised as experimental design type. Figure 4.2.6.13 shows two examples in the 1970s that represent the settings of experimental devices. Such drawings belong to the tradition of journals in chemistry and biology. Since the 1980s, drawings of experimental settings obviously decreased in the object type, while representations of macromolecular structures increased quickly. Meanwhile, there are some slightly special cases. Figure 4.2.6.14 contains two diagrams from different papers in 2003. Figure 4.2.6.14A is about a protein chimera, and Figure 4.2.6.14B represents an apoptotic protein complex. Their artistic effects are more advanced than typical diagrams of molecular structures, but their compositions and the ideas conveyed do not go beyond the norms of this type. The only special feature of them is the graphic effects that possibly result from the rapidly improving graphic tools in the early 2000s.

Occasionally, there are cases of rare styles of representing macromolecular structures. Figures 4.2.6.15 and 4.2.6.16 show the only two cases different from typical linear arrangements of letter abbreviations. Figure 4.2.6.15 is about the annealing of DNAzyme and mRNA from experimental animals. It displays the sequences and the structures of the genetic materials. Figure 4.2.6.16 displays the structures of an antisense RNA (on the left) used to prevent translation and an RNA-ribozyme complex predicted by computer programmes. In these two figures, a kind of RNA pattern is vividly represented by the hairpin shapes. The pattern is called “hairpin loop” and usually comprised of single-strand RNAs or DNAs. Thus, representing RNA sequences with loops in a hairpin shape is visually resembling the shape of the actual object, just like representing DNA sequences with linear arrangements. This seemingly odd style in fact serves as a visual resemblance to the entity, and visual resemblance is a traditional way of making diagrams in biology.

The ED type shows relatively higher variance in both style and theme. The dominant theme centres on genetic manipulation procedures, which are typically represented by a series of changing structures of genetic materials (as seen in the other journals). This dominance of biotechnology diagrams in the ED type is consistent with the large coverage of genetic structures diagrams in the object type. There are other themes, too. Figure 4.2.6.17 vividly illustrates an experimental device (chamber slides). The use of words is reduced to a minimum. The alphabetic letters only indicate the sequence of procedures. Without the caption, the image provides very limited information about the procedures. The message is more likely to be understood by the viewer with background knowledge about the use of “chamber slides”: (1) seed cells onto the slides, (2) then the cells form a monolayer. The trained viewer may also notice that, in *b*, the cells are settled on one side of the slide because of gravity. However, the difference between the high and low water levels in *c* and *d* does not make the procedures any clearer, where the procedures are (1) washing the cell-labelling solution with buffer saline and then (2) culturing the cells with untreated medium. This diagram conveys the message clearly and efficiently only to the trained viewer who knows the device and can interpret the meaning of the dotted line (cell monolayer).

Figure 4.2.6.18 demonstrates an improvement of the visual language in the ED type. Figure 4.2.6.18A is published in 2004, and Figure 4.2.6.18B is from 1987. Comparing their uses of arrows shows that 4.2.6.18A conveys information more concisely than 4.2.6.18B. The meaning of the arrows in 4.2.6.18A is cytokeratin cleavage by enzyme caspase-3. This is not ambiguous. But the arrows in 4.2.6.18B can be confusing due to their multiple meanings: sample collecting, fixation, and indication of different treatments at specific timings. The variety of the arrow length and the uniform arrow form cause much ambiguity. Confusion also comes from the absence of unit (kDa), so only the informed viewer knows the unit of the numbers. Apart from their differences in the use of visual vocabulary, the graphic effects in 4.2.6.18A is more sophisticated than 4.2.6.18B. This

probably parallels the spread of digital graphic technology. Such obvious improvements of graphic effects in the 2000s are seen in almost all diagram types in all the journals surveyed.

Diagrams in the chemical structure (CS) type have two common features. Firstly, they are all illustrations of chemical compounds used in experiments on potential cancer treatments, either via drug uptake or dietary alteration. Secondly, all the compounds are artificially synthetic and, in most of the cases, commercially available. This ensures that the experimental results are reproducible in other local settings. Some of the synthetic drugs are derived from natural compounds. Such an overwhelming prevalence of synthetic and commercial cancer-treating reagents in the CS type cannot be surprising in this journal, given the aforementioned emphasis upon frontier discoveries in therapeutics. The very relationship between apoptosis and cancer is that excessive survival of cells (which are abnormally resistant to apoptosis) tends to lead to carcinogenesis. Therefore, apoptosis papers sampled from a cancer-focusing journal tend to be about inducing death of cancer cells. The means of induction is treating the cells with novel compounds of interest. The novel compounds need to be visually highlighted. This highlighting may result in both the impressive presence of representations of chemicals (including reagents and nutrients) and the relatively higher proportion of the CS type in *Cancer Research* than in the other journals.

The “other” (miscellaneous) type contains only one case, which is a pedigree diagram displaying the experimental results of an X-irradiation of cells (Figure 4.2.6.19). The recorded times of cell changes (either undergoing mitosis or starting apoptosis) are represented by branched lines. The meaning of the numbers in this image is vague. Without the caption, it is hard to read whether these are the cell numbers or the timings. Only the initial treatment (X-ray) is well-conveyed. Unlike normal ways of displaying data, the description of experimental conditions in this diagram is minimal. The very rare frequency of such ambiguous diagrams may imply that such a style is not effective in conveying experimental results. This diagram is creative in the sense of using pedigree trees to order the observations (cell changes), but such creativity can interfere with the effectiveness of communication.

The mechanism diagrams in *Cancer Research* exhibit great variety in style. When comparing the diagrams before and after 2000, some evolutionary changes are noticeable. Early diagrams, having relatively simpler visual elements, tend to employ traditional compositions and styles, such as flow charts and hand-drawings. Later diagrams not only embody the obvious impact of novel graphic tools but also contain more complex contents. Moreover, some later cases are more experimental in visual configuration. Figure 4.2.6.20 is a mechanism diagram in 1995. This basic, flow-chart composition has certain visual similarities with the pedigree diagram in Figure 4.2.6.19. Apart from the black-and-white colour, which is very likely due to the state of technology in the 1990s, the visual elements and the composition are also basic. Words and arrows are the only two elements. While the branching pathways concisely convey the cascades of reactions, the multiple dimensions of the mechanism are unclear in such a composition. The composition is a collection of linear narrations, where only the trained viewer may recognise the multiple interrelationships amongst the components.

Changes in the visual language before 2000 seem to occur slowly. Figure 4.2.6.21B presents a typical style of displaying a series of linear reactions. Apart from the words, this 1989 diagram has two elements: the double helix and the triangle. The former is a simplified icon of DNA, which has been widely used for a long time (perhaps since the original conceptualisation of the double helix structure of DNA<sup>72</sup>). The use of black triangle for representing dNTP is possibly arbitrary. Figure

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<sup>72</sup> The emergence and popularisation of the DNA icon is an interesting topic. Future study may explore the interplay between the spread of knowledge of DNA structure and the development of DNA icons. If this interplay exists, it can shed light on some points: the establishment of visual convention within and outside scientific communities, the relationships between visual convention and knowledge transfer, and so on.

4.2.6.21A has a flow-chart style that is slightly more complex than Figure 4.2.6.20. In this 1985 diagram, the cross-linking arrows show the relationships between some pathways. Generally, they have two meanings: (a) temporal sequence, (b) multi-field causalities (primary events, cellular consequence, and form of cell death). The process from “DNA breakage” to “chromosome aberrations” exemplifies the former meaning. The process from “DNA synthesis inhibited” to both “DNA breakage” and “aberration re-replication” exemplifies the latter meaning. Such multi-field causalities are also seen in Figure 4.2.6.20. While there are ten years between these two flow charts, there is almost no difference between these two diagrams in terms of the complexity of style, visual element, and composition. Interestingly, the complexity of ideas about multi-level structures of mechanisms has grown during this period.

Both Figure 4.2.6.22 and 4.2.6.23B are examples of traditional hand-drawing style. Similar drawing styles and typewriter fonts can be found in earlier papers in the other journals and in other biological fields. Figure 4.2.6.22 is highly object-centred, displaying a cell and its ion exchangers/transporters, if the causal relationship between pH falling and ion transport was not shown by the simple elements. Similarly, Figure 4.2.6.23B is also a mechanism diagram that is object-centred. There are several simple rectilinear processes without details, such as the formation of neoplastic nodules. But the lack of details is probably due to the emphasis on the alteration of phenotypic expression. This is a relatively compact configuration, as it distinguishes two types of expression with two kinds of colouration. Such compact configurations are not quite experimental in its period (1990). Figure 4.2.6.23A is an ED diagram from the same paper and exhibits visual consistency with 4.2.6.23B. It also has a basic style of representation. The overuse of numbers on the time scale is a somehow redundant design.

Figure 4.2.6.24 compares traditional and novel visual languages. This comparison suggests that the visual evolution of mechanism diagrams results from a convergence of novel scientific ideas and novel graphic tools. Figure 4.2.6.24A is published in 1992, and 4.2.6.24B is in 2001. The differences between their visual languages embed both the evolution of graphic technologies and the impact of new data on visual representation. New technologies allow 4.2.6.24B to represent the irregular structures of molecules with much freedom and more ornamental effects than the hand-drawing style in 4.2.6.24A. Meanwhile, new discoveries in molecular structures may have inspired the creation of novel elements that resemble the entities, eg. the ball-chain icon of actin filaments in Figure 4.2.6.24B. Advanced research tools provide more resources for visualising molecular and smaller entities at finer levels. For example, atomic-level exploration of the structure of the actin family burgeoned in the 1990s, when an atomic model of F-actin filament was published in *Nature* (1990)<sup>73</sup>. On the right side of 4.2.6.24B, there is a protein at the intercellular tight junction (TJ), ie. occludin whose role and structure are novel discoveries at that time. These discoveries are tied to novel biological methods arising since the late 1980s<sup>74</sup>. At the same time, advanced graphic technologies have been facilitating the creation of new visual elements. The roughly parallel advances of these two kinds of technology converge at the visual evolution of mechanism diagrams. Such a convergence also has an impact on existing visual conventions. For example, the cell membrane in Figure 4.2.6.24B is almost an extravagant use of graphic technology. Neither the knowledge of lipid bilayer structure nor such a way of representing it is novel. Delineating this structure in detail has limited (if any) technical function in representing the overall mechanism.

Figure 4.2.6.25 is another demonstrative example of the impact of advanced technology. The composition and the style of this diagram are both typical of mechanism diagrams in contemporary bioscience. The characteristics of such composition and style include: (1) representing crosslinks between the acting units (molecules), the loci (cell organelles), and activities; (2) containing multi-

<sup>73</sup> Holmes et al., 1990, 44-49.

<sup>74</sup> For one of the early papers recognising occludin and the techniques it employs, see Furuse et al., 1993.

dimensionality implied by the crosslinks, and (3) using multiple visual elements. Unlike Figure 4.2.6.24B, the visual elements do not resemble the shapes or structures of the molecules. The use of these representational icons seems as arbitrary as the use of the black triangles in Figure 4.2.6.21B. Nonetheless, the icons in Figure 4.2.6.25 show certain degrees of sophistication. This is plausibly due to the improvement of graphic tools that makes the process of production and manipulation of iconic resources easier than early years (Briscoe, 1990). The manipulation can include multiplication, uniform copying, and arranging basic shapes in complicated ways. The advanced technology also produces fine designs of icons, eg. the Bcl-2/Bcl-X<sub>L</sub> complex on the mitochondria.

The following figures present some special cases of mechanism diagrams. They can be roughly divided into three kinds. The first kind has a high proportion of non-biological contents, such as chemistry. The second kind embodies creative thinking in terms of configuring heterogeneous elements and information sources. The third kind is about visual experiment on using very simple ways to convey complicated information.

Figure 4.2.6.26 and 4.2.6.27 belong to the first kind. These two mechanism diagrams are very similar to representations of chemical reactions. Their major components are both about chemistry, making them at first glance look like the CS type or the miscellaneous type. Only one or few arrows and words indicate the transitions from chemistry to biology. The arrows pointing to biological reactions, such as “DNA” (Figure 4.2.6.26) and “DNA damage” (Figure 4.2.6.27), indicate that the reactions go beyond the sphere of chemistry and enter biology. Namely, the chemical and biological *perspectives* are integrated by these simple elements. This integration at the same time designates a *purpose* to the chemical reactions—to cause apoptosis. The link between the chemical and biological perspectives becomes causal due to this integration. Therefore, the diagrams as wholes: (1) are syntheses of perspectives of two disciplines and (2) explain the phenomena. These two points make them biological mechanism diagrams.

Figure 4.2.6.28 to 4.2.6.30 present the second kind of rarities. These are creative attempts to incorporate many perspectives into the representations. They possess different degrees of information synthesis. Figure 4.2.6.28 shows a set of pathways induced by different treatments (or, from another aspect, in different environments). Three pathways are rectilinearly displayed. Basic geometric shapes are used to represent the entities and the loci of activities. The original diagram is printed in black and white. So far, this 1993 diagram shows typical features of early mechanism diagrams. However, at the convergence of the three pathways, an experimental photograph of DNA gel electrophoresis, instead of a drawing or some words, is inserted to represent “cell death”. In apoptotic cells, DNA is cleaved into fragments. Thus DNA samples extracted from apoptotic cells appear as discontinuous “ladders” in gel electrophoresis. “Laddering” of DNA is representative of DNA fragmentation, serving as a visual indicator and a hallmark of apoptosis. In this diagram, the picture of DNA ladders is used as an icon for cell death. This embedding of data image is different from many other mechanism diagrams in this journal and the other journals. It shows that data images can be employed as iconic elements. Although the resolution of the photograph is limited by the state of technology, this diagram demonstrates creative thinking in the way of constructing mechanism diagrams. Section 5.5.3 will use this example and similar ones to argue that integration of data images and diagrams change both the epistemic roles and the signifying functions of the data images.

Figure 4.2.6.29 shows a similar attempt to integrate data images and drawings of mechanistic models. It differs from Figure 4.2.6.28 in the way that the data images (the two charts) have a more active role: they present a phenomenon that is to be explained<sup>75</sup>. The upper panel contains the charts

<sup>75</sup> One might assume that, in a broad sense, the DNA fragmentation phenomenon is also to be explained by the pathways drawn. This assumption comes from the causal connection between the pathways and DNA fragmentation.

plotting the changing density of chloride ion current from one condition to another. The lower panel contains two small diagrams illustrating the underlying mechanisms of the ion current increase. The scientific message here is that the over-expression of apoptotic protein Bcl-2 leads to the increase of chloride ion current in a hypotonic (swelling) condition of a cell. The models provide explanations for the recorded data as follows. Firstly, the enhanced expression of chloride ion channels (VRAC) are represented simply by the increased number of the “channel icons”. Secondly, the changed amount of Bcl-2 from baseline level to over-expressed level is also straightforwardly depicted. Via serial pathways, over-expression of Bcl-2 leads to a loosening of inhibition of VRAC activation under a hypotonic condition. The indicating arrow at the bottom again emphasises the cause of the phenomenon seen in the data charts, ie. Bcl-2 over-expression. Just beneath the data, there are the visualisations of the explanations. The visualisations are cartoon-like, containing various specially-designed icons. A time axis implicitly runs through the process from left to right. The implied passage of time can be read from not only the sequential “cartoons” but also the charting of data. The synthesis of data and small diagrams provides two directions of reading this figure as a whole—the model explains the data, and the data evidences the model.

Figure 4.2.6.30 integrates information from the experimental design, the data, and a hypothetical mechanism. This is a 2003 diagram whose visual elements are as basic as early diagrams. Its arrangement of the elements is also a basic flow-chart layout. But both the meanings of these elements and the way they are configured are sophisticated. Starting with the experimental treatment (SAMC) on the cells, the viewer's eye is directed into a special space separated by simple lines that represent the cell membrane. The space is special because of the coexistence of the three packets of information. The viewer is required to carefully distinguish between these three: experimental manipulation (such as artificial interference), experimental results (such as MT (microtubule) depolymerisation), and the hypothetical mechanism (which includes the pathway from JNK1 activation to apoptosis). The message of this diagram actually needs to be interpreted via inter-referencing between these three packets of information, where the time axis interlaces them. Compared with many other mechanism diagrams that contextualise the discoveries in big pictures, Figure 4.2.6.30 focuses on a particular topic and has a relatively “local” scope. This mechanism diagram does not concern much interaction between the novel findings and the existing knowledge. Instead, it visually contextualises the findings in a specific practice. This diagram is creative in the way of synthesising heterogeneous information and turning the integrated whole into a new meaningful one. Section 5.5 and 5.6 will discuss how mechanism diagrams synthesise heterogeneous components and generate novel meanings of the wholes. Thus this diagram, while having a rare configuration, is in fact a very demonstrative example of such features.

Figure 4.2.6.31 shows the third kind of rarity: conveying complex messages by very simple and creative visual language. The original paper is about a hypothetically shared pathway between apoptotic regression of prostate and proto-oncogenetic progression of prostate cells (eg. expression of cancer-related genes). This diagram pictures the author's explanation for this paradox, ie. the co-development of regression and progression, and cell death and proliferation (Colombel et al. 1992). The main part of the diagram is a thick circle representing a cell cycle, with highly abbreviated letters that can only be deciphered with background knowledge. These letters (S, G<sub>1</sub>, etc.) stand for five phases of the cell cycle. In this paper, an experimental surgery is conducted at G<sub>0</sub> phase (the

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However, the purpose of inserting the DNA photograph is to represent the occurrence of apoptosis. The paper (Figure 4.2.6.28 from Walton et al. 1993) studies some specific pathways in apoptosis and chooses DNA fragmentation as an indicator. The inserted data can be any other captured apoptotic phenomena. The observation of DNA laddering is not an exclusive one but chosen to represent apoptosis. Given the available technology at that time, it is possible that DNA fragmentation is chosen because it is relatively easy to quantify. Thus the “progress of death” can be measured.

start of the cell cycle) to castrate the animals. Then, at a time between S (the phase of DNA replication) and G<sub>2</sub> (the phase of cell growth), apoptosis is observed. Using a circular shape to represent the cell cycle is common in biological visualisation. A circle can show both (1) the different phases and (2) that the process is circular and repeating. By using this shape and adding a few elements (words and arrows) to it, this diagram concisely expresses both the sequential development in prostate cells through the early phases of cell cycle and the causal link between castration and apoptosis.

Nevertheless, concise visual language for the experts can be obscure to non-experts. This diagram is difficult to understand for a viewer without the knowledge of the phenomenon that both cell death and oncogene expression happen after prostate removal. The interpretation of this diagram requires familiarity with some specific areas, such as cell cycle, prostate epithelial cells, and prognosis of prostate cancer surgery. Thus a non-expert viewer (even from other biological fields) might not even notice what the hypothesis of this paper is. Also, this diagram is simple because the mechanism of interest is relatively simple. It is from the early 1990s and does not involve many molecules and processes, containing mainly the shared pathway between cell growth and death. In this sense, this diagram could be drawn linearly, but the author chooses the cell cycle shape. Possible explanations include visual convention in biology and aesthetic consideration.

Figure 4.2.6.32 to 4.2.6.34 provide examples of emphasising the mitochondria in diagrams composed of very simple elements. This kind of visual emphasis has been observed in the previous journals. As Section 4.2.3 has described, in *Cell Death and Differentiation*, mechanism diagrams containing very basic visual elements and having simple compositions tend to visualise the mitochondria by specially designed icons. Usually, the mitochondria icon<sup>76</sup> is also larger than the other elements. Although the mitochondria *are* central to apoptosis, such an emphasis still seems unnecessary in some cases. The mitochondria and the related processes could be represented by basic elements, without affecting the conveyance of message. In Figure 4.2.6.32, the mitochondria is not completely drawn, but it is visually significant in size and appearance than the other components. Indeed, in apoptosis, Bax protein is located on the mitochondrial membrane, and cytochrome c is released from it. But removing this mitochondria icon would not change the function of the diagram to represent the interactions between these molecules.

On the other hand, there are cases where the mitochondria have to be visually significant. Figure 4.2.6.33 is about the mechanisms that mostly happen within and on the mitochondria. In this case, the mitochondria are the loci of events. This diagram contains two large mitochondria, which are the most figurative components. Figure 4.2.6.32 and 4.2.6.33 have an obvious contrast to each other in terms of their main messages. Figure 4.2.6.32 displays the events that mainly happen in the cytosol, and Figure 4.2.6.33 concerns the mitochondrial events. It is then worth asking why, in both diagrams, the only large and most figurative elements are the icons of mitochondria, when the other elements are basic and the compositions are simple.

Figure 4.2.6.34 has a special icon already seen in Figure 4.2.3.14: the scissors. With regard to employing everyday visual elements, it is also similar to Figure 4.2.6.35 and 4.2.6.36. Similar to Figure 4.2.3.14, the scissors represent “cleavage” (or cutting). The cross icon represents “prevention”, (ie. preventing the pathway leading to protein expression from proceeding). But the scissors and the cross have some similarities in terms of their appearance and the way they are imposed on the molecules. In biological diagrams, inhibition and prevention are normally

76 “Mitochondria” is a plural term and “mitochondrion” is singular. A cell has more than one set of mitochondrial structures. Normally, the term “mitochondria” is used as singular, for it also represents the cell organelle as a whole. In the case when a particular one is referred to, eg. in a microscopic image, the real singular “mitochondrion” is used.

represented by a special arrow whose arrowhead is a bar (a stop sign). Here, the meaning of the cross is likely to be confused with cleavage. Nonetheless, the cross plays a role in explaining the difference between the active sites of the treatments: in the middle part of the diagram, NF $\kappa$ B is suppressed and thus the downstream c-FLIP expression is prevented; in the right part, NF $\kappa$ B is not suppressed, while the treatment blocked its route to c-FLIP expression. In this regard, the scissors and the cross have distinguishable functions. But only the informed viewer can interpret this distinction. It is arguable that the scissors add some values other than effectiveness of communication. For example, they make the model look interestingly vivid.

Figures 4.2.6.35 and 4.2.6.36 present more examples of metaphorical signs seen in everyday life. These are also examples of the “fun” face of technical communication in bioscience. The emotional faces in Figure 4.2.6.35 clearly show the process from health to death, portraying the cell as a conscious character. The cells are imposed a personality. Usually, such vividness offers more fun than technical information. Removing the emotional expressions does not alter the key message of the diagram. In Figure 4.2.6.36, the tombstone and the “epitaph” have a similar function. The tombstone obviously adds vividness to the cell events. But the epitaph in fact has a scientific meaning, though in a non-technical form. The tombstone sign catches the eye, when the other visual elements are either resemblances to the entities (the mitochondria icon) or very simple (the basic graphs). This sign is seldom used in technical diagrams but still is a familiar, everyday sign. Thus it appears especially notable. The epitaph is put in capital letters. This also distinguishes it from the other words in the diagram and turns the scientific meaning into a playful metaphor.

Such playful ingredients do not appear frequently. In this journal, they are as rare as the other creative cases. However, there are differences between the journals. In *Nature Reviews MCB*, death skulls are frequently found. It is unclear why the authors of these apoptosis papers incorporate these interesting everyday elements into their diagrams, which are to be released on professional media. Using these elements does not add much scientific value to the visualisations. Moreover, using such elements does not necessarily attract a wider audience, as the reader who views these diagrams tends to focus on the scientific messages but not the aesthetics and the fun creations. Yet such elements do add metaphorical features to the diagrams: they bring the technical contents to life—especially when the contents are about dynamic mechanisms—without affecting the accuracy of communication. Section 5.3.2 will discuss more about these non-specialist elements, as well as their link to developing technical visual language. Future study may also examine whether or not such incorporation of everyday metaphors into diagrams is specific to the apoptosis field. Above all, apoptosis is *cell suicide*. The concept itself is capable of provoking imagination. So is the term *apoptosis* itself, which has a perfectly metaphorical etymology rooted in the Greek language, namely, the natural fall of leaves in autumn.

## 4.2.7 Cell

Figure 4.2.7.1 presents the number of search results and samples from *Cell*. The number of analysed papers is in Figure 4.2.7.2. Only a small number of papers were omitted, for most of the search results are relevant to my subject matter<sup>77</sup>.

As no diagram appears in the 1970s (only 3 apoptosis papers), the calculation of D/VI started at 1980 (Figure 4.2.7.3). Through 25 years, the D/VIs remains considerably steady. The small difference between the D/VIs in the 1980s and the 1990s can be ignored, when the large variation in

<sup>77</sup> In the other journals surveyed, this is not always the case.

the 1980s is considered. The 1980s group has an obvious variation due to the very small sample size (5 papers). In general, the D/VI in *Cell* is “middle to high” amongst all the journals surveyed (Figure 4.2.6.4. An overview of all the journals is provided in Figure 5.1, and Section 5.1.2 will interpret it.).

The total numbers of the five diagram types in different decades are shown in Figure 4.2.7.4. Similarly to the other journals, object and mechanism are the two most prevalent ones, and the other three types remain minor. But a closer look shows that the object type is the only consistently dominant type since the 1980s. On the other hand, the mechanism type exhibits a persistent growth. Having initially been less prevalent in the 1980s, the mechanism type has become one of the two prevalent types in the 1990s and then surpassed the object type in the 2000s. The changes in proportion of the five types (Figure 4.2.7.5 and 4.2.7.6) clearly show the paralleled shifts between the object and mechanism types. While the object type reaches the peak proportion in the 1990s and then drops in the 2000s, the mechanism type is steadily growing in a nearly linear manner (Figure 4.2.7.6).

Meanwhile, the relative changes in frequency of the two prevalent types exhibit a pair of nearly inverse patterns. Figure 4.2.7.7 separately shows the gradual decrease of frequency of object diagrams and the gradual increase of frequency of mechanism diagrams. From the 1990s to the 2000s, the frequency of the object type declines significantly. The frequency of the mechanism type increases significantly from the 1980s to 1990s and then keeps growing in the 2000s. To illustrate these patterns more clearly, Figure 4.2.7.8 plots the changes of frequency of the five types.

Figure 4.2.7.9 is a scatter plotting of the frequencies of the two prevalent types, providing a rough picture of the distribution of the individual ratios (ie. the D/VI of a diagram type in an individual paper) from 1980 to 2005. Figure 4.2.7.10 sketches the average frequencies of different diagram types by year from 1980 to 2005. The years are assigned as numbers from 1 to 25. This is to simplify the calculation, minimising the effect of numbers of the year<sup>78</sup> on the function parameters. Generally, the decrease of frequency of object diagrams and the increase of frequency of mechanism diagrams are both gradual, resulting from the continually changing composition of the sample set of papers through the period. Thus the correlation coefficients are quite low. Despite the low  $R^2$  values, this sketchy comparison indicates the paired patterns of decreasing objects and increasing mechanisms. This pair of patterns is more obvious in Figure 4.2.7.11, when the trend lines appear more linear because the calculation was further simplified by using the average ratio in each decade. Figure 4.2.7.11 is an over-simplified scenario and used here just for pointing out the dramatic changes. The implication is important and intriguing: in *Cell*, the focus of interest in visual representation has shifted from objects to mechanisms.

From this paragraph onwards I present the qualitative results. The majority of object diagrams in *Cell* are again about macromolecular structures. The forms include letter abbreviations and schematic depictions of genes and amino acids and/or protein alignments. Slightly different from the other journals, the remaining object diagrams in *Cell* pay much attention to biological structures than to experimental settings. Biological structures are in the form of either anatomical or histological representations. Figure 4.2.7.12 shows a histological drawing in part A (bone tissues) and two anatomical drawings in part B (the embryonic germ layers) and part C (a nematode). In *Cell*, there is a notable presence of histological and anatomical diagrams that concern embryonic development or individual growth. Figure 4.2.7.13 and 4.2.7.14 provide three examples of this kind. An explanation is the importance of apoptosis during embryonic development, individual growth, and homeostasis (cell renewal and maintenance). Also, it is well-known that anatomy and histology both have a tradition of heavy reliance upon visualisation of objects. Visualisation in these two

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78 For example, 1980 should not count as one thousand nine hundreds eighty.



disciplines is an essential component of apprenticeship training, knowledge propagation, and specialist communication. It should not be surprising that apoptosis papers studying cell death from anatomical and histological perspectives present so many drawings of objects. It is also interesting that, despite the journal title, many apoptosis papers in this journal concern the levels higher than the cellular and the molecular, ie. tissue, organ, and organism.

Figure 4.2.7.15Left is another example of anatomical drawing and also a case of modular use of visual elements. It illustrates the relative spatial arrangements of two bundles of mossy fibres and their projections (mossy fibre is a specific kind of hippocampal nerve axon). In this simplified schema of axon growth, the arrows indicate the routes of projection. Interestingly, later in the same paper, part of this simplified diagram of hippocampus cell layer section is embedded in a diagram of experimental design (Figure 4.2.7.15Right). In this embedding, some elements are removed: the red lines representing the bundles, the red arrows representing the projection, and the letters representing different areas in the hippocampus (namely, CA: cornu ammonis; DG: dentate gyrus). Only the “background” (the schematic drawing of the hippocampus) is used. The curvy grey lines are common elements in drawings of the hippocampus and are kept because they resemble the observations of hippocampal tissue section. In sum, the simplified hippocampus diagram is re-used in another diagram for a different purpose, as if it is a *template* icon of hippocampus. This renders a visual consistency throughout the paper. Moreover, because this schematic drawing resembles the photograph of a hippocampus section, the visual consistency unites three different sources of research images (photographs, object diagrams, and ED diagrams).

In the same paper, there is a diagram which does not possess this consistency. It is a combination of drawings and photographs (Figure 4.2.7.16). The explanation for the absence of the “template” icon is simple: this diagram is a closer observation of a hippocampus section and thus has a higher magnification. At first glance, the diagrams seem to be transformed *from* the photographs, given the similarities in component, colour pattern, and composition. If this is true, it is a photo-to-diagram rendering argued by Lynch (1990). However, these diagrams are not created after the photographs. Instead, they represent the “predicted results” (Bagri et al. 2003) of double fluorescence immunostaining. The two diagrams are predictions for the results of staining the samples in two different experiments. Microscopic photography was used to detect the staining of nerve fibres in certain areas of the hippocampus. These nerve fibres are stained as green (wild type), red (mutant), or yellow (the merging of red and green fluorescent stains, representing wild type nerve bundles that may be defective due to mutation). In other words, the diagrams were created either *before* or *at the same time with* the production of the photographs. Even if the latter is true, the diagrams were intended to be read prior to reading the photographs.

Therefore, the drawing in Figure 4.2.7.16 is not a transformative rendering from photograph. Indeed, the small diagrams seemingly show the traces of serial modifications of photographs, such as highlighting the key parts and degrading the irrelevant background. But the information in these two diagrams has an instructional function to advise the viewer *what to see* in the data images. It is a predictive preview of the result but not a diagrammed or transformed version of the result. This image is a case of “reverse transformative rendering”. The diagrams are probably transformative renderings from some previous photographs, but they now serve as a preview of future results. This case shows that the relationships between data images and diagrams in biological sciences vary with the practice. Section 5.2 will discuss the multiple possibilities of data-diagram relationship and argues that one-way transformation is not always the case of making biological diagrams.

Figures 4.2.7.17 to 4.2.7.19 are examples of the experimental design (ED) type. In *Cell*, the majority of this type are representations of genetic recombination, which are also common in the other journals. ED diagrams in *Cell* have no typical style and are creative in terms of element and composition. Figure 4.2.7.17A is simple and quite object-centred. Figure 4.2.7.17B is also object-

centred, while having multiple visual elements. Figure 4.2.7.17C is an early (1985) example of representation of gene construction. Figure 4.2.7.17D exemplifies a traditional style of ED diagram, which normally employs flow charts and linear compositions.

Creativity of the ED diagrams is seen in some subtle details. In Figure 4.2.7.18A, simply by bending the lines, which represent DNA single strands at different locations and in different forms, the procedures of artificially forming Holliday junctions (mobile structures of DNA) are clearly conveyed. The DNA strands annealing assays are represented by the plus signs, and the directions of assays are straightforwardly shown by the arrows. The use of words is limited, symbolising only the difference between labelled (S1) and unlabelled (S2) DNA strands, as well as the assay products. The assay products are 3WJ and 4WJ, meaning three-way and four-way junctions. They are actually represented by the designed icons, making the words somewhat redundant. Note that all these creative elements are quite conventional in molecular biological diagrams (eg. representing a Holliday junction with a bent line, and representing DNA annealing by a plus sign). This diagram does not have novel visual elements, but it creatively composes conventional elements in a concise way that facilitates the visual communication.

Figure 4.2.7.18B uses similar elements seen in 4.2.7.18A and is another example of composing conventional elements in a communicatively effective way. The elements it uses are even more basic. The words describe (1) the characteristic of the cells, (2) the experimental conditions (time durations and reagents of treatment) and process (cell sorting), and (3) the results of the process. Two forms of arrows respectively represent the instructional steps and the direction of experimental process. Two different states of cells are distinguished by two different colouring patterns of the same icon (circle). Such a style may be one of the most conventional ways of representing an experimental design. There are not many graphic components, as the words describe most of the information. The limited and creative use of graphic components, such as different colouring patterns of the circles, constructs a concise visual vocabulary.

Figure 4.2.7.19 displays a series of illustrations of electrophoresis. The graphic parts are simplified and schematic drawings of the experimental setting. A few words are added for describing the objects and the stages. Interestingly, the information about SDS-PAGE electrophoresis is actually as abstract as the cell differentiation process in Figure 4.2.7.18B, but these two figures are very different in their use of descriptive graphics. Figure 4.2.7.18B mainly uses words and limits the use of graphics, whereas Figure 4.2.7.19 mainly uses iconographic elements to describe the procedures. There are three possible explanations for this difference: (1) the electrophoresis apparatus is easier to simplify and transform to schematic diagrams, (2) an image of electrophoresis can be more visually impressive than the cell sorting process, and (3) the expected results of the two experiments have different forms, where cell sorting is numerical (Figure 4.2.7.18B) and gel electrophoresis renders an image (Figure 4.2.7.19). In Figure 4.2.7.18B, picturing the treatment processes can be redundant. Also, the appearance and the concepts of cell sorting machine (flow cytometry) appear to have fewer visual features.

The “other” (miscellaneous) type is as rare as in the other journals. The majority are dendrograms. Only one case is not dendrogram and will be discussed in the following paragraph. The dendrograms represent either results of phylogenetic analysis or hierarchical relationships between molecules within a specific family. Figure 4.2.7.20A shows the alignment of kinases in a special enzyme subfamily. Figure 4.2.7.20B displays evolutionary conservations of a particular protein domain in different species, as well as their evolutionary relations with each other. Figure 4.2.7.20C displays the results of a screening analysis of cells. Figure 4.2.7.20D represents the lineages of cells that either survive or undergo apoptosis in accordance with either the reduction or the absence/presence of an apoptotic gene, *ced-3*. Figure 4.2.7.20A and 4.2.7.20B focus on genealogy of the molecules, while 4.2.7.20C and 4.2.7.20D focus on clustering of discrete experimental

results. Yet they are similar in visual style, for they all display the relationships in the form of branches. Their difference lies in whether the relationships are structural (Figure 4.2.7.20A), evolutionary (4.2.7.20B), temporal and causal (4.2.7.20C), or ancestor-descendant (4.2.7.20D). Despite their visual similarity, these diagrams are not homogeneous in terms of the meanings imposed on the branching configuration.

Figure 4.2.7.21 presents the only case of non-dendrogram in the “other” type. It is a schematic representation of the observation of enzymatic activities during an experiment. While the overall composition of the elements resembles—maybe misleadingly—a well-ordered and structured bar chart of quantitative data, the original caption of this diagram clarifies that this is not a reflection of the actual data. It states, “the height of the bars is symbolic and does not reflect the actual scale of increase in dNTP pools. The separation between active and inactive RNR molecules does not represent their different localizations within the cells. It is used only to emphasize the correlation between active molecules and the levels of dNTPs.”<sup>79</sup> No number of dNTP level is given on the vertical axis, and the widths of cell cycle phases on the horizontal axis do not represent the durations of the actual phases. The adjacent bars are not even continual and sequential: two conditions (i.e. S phase and DNA damage occurrence) of two cell types (wild and mutant) are drawn by turns. Above all, this chart graph has no scale. The numbers of the shapes are not in line with the actual data. The black squares, the grey crescent-shaped graphs, and the red and green graphs respectively represent different molecules. But their repeating patterns do not have quantitative meanings.

So the message is clear: this diagram provides a general and conceptual schema, instead of quantitative information. Based on this visualised schema, the viewer can interpret the relative changes of the molecules along cell cycle progression. Here I explain the message. Before the S phase of the cell cycle, most of the enzyme RNR is inactivated by its inhibitor (Sml1). When the cell cycle begins, the RNR level is increasingly inhibited by its catalytic product dNTP via a mechanism called “feedback inhibition”. In wild-type cells, a feedback inhibition of dNTP synthesis makes it difficult to recover from DNA damage. The cells undergo apoptosis. But in artificial mutant cells, whose feedback inhibitory route is blocked due to the mutation of the allosteric site (i.e. the active site) in RNR, dNTP synthesis continues. As a result, the cell survival rate is enhanced. From this, it is easy to see that the synthesis of dNTP is important to cell proliferation. In Figure 4.2.7.21, the build-up of black squares represents the accumulation of dNTP due to relaxation of dNTP synthesis from feedback inhibition. From the S phase to the induction of damaged DNA, the number of “mutant” signs increases and the number of “wild type” signs decreases. These relative changes suggest survival of mutant cells and death of wild type cells.

In sum, this figure borrows a composition from bar charts. Such a composition is impressive for its well-ordered structure. The number of the signs does not represent the actual quantity of molecules, but it helps the viewer recognise the ideas of “many” and “few” and the relative changes in quantity. However, a visual experiment like this diagram may be risky in terms of communicative effectiveness, for it deviates from visual conventions and causes ambiguity. It makes very novel meanings out of visual conventions, so the viewer may need supplemental information to overcome the confusion. In the original paper, this diagram is accompanied by a long text describing the phenomena. The original caption also includes a clarification to avoid confusion (as mentioned in the previous paragraph).

Mechanism diagrams in *Cell* exhibit no obvious evolution in styles. Traditional styles, basic elements, and linear compositions coexist with creative styles, complicated compositions, and novel visual elements. Nonetheless, in the 2000s, the richness of visual elements somewhat grows, and the dimensionality embedded somewhat multiplies.

<sup>79</sup> Chabes et al., 2003, 398, Figure 5.

Figure 4.2.7.22 has a linear composition. This should be due to that the key message is a linear pathway. The circles can be confusing due to an unclear switch of meanings. These circles have two meanings: the left two circles stand for a progressively dying cell. In the right half, the two circles represent engulfing cells that “swallow” the dead cells. While the left two and the right two circles look similar, they represent two different kinds of cells. The meaning of the left two circles turns out to be represented by a small circle embedded in the first right circle. There is no clear clue to this switch of meanings, except for some descriptive elements, ie. the cross on the second left circle representing the death and the words and lines indicating the names of the cells. In sum, there is no clear rule for the plurality of the meanings of the circles. This simple linear composition does not necessarily lead to effective communication.

There are cases of object-centred mechanism diagrams as already seen in the previous sections. The objects are the most significant parts. Elements not representing objects are either smaller in size or made less visible by some graphic effects. Object-centred mechanism diagrams in this journal are varied in style. For example, Figure 4.2.7.23 shows three diagrams from two papers. While Figure 4.2.7.23A and 4.2.7.23B are from two different papers, they employ similar elements, eg. squares, ellipses, arrows, and labelling words. They are representations of the bindings between proteins and genes, as well as the actions and interactions. The left and the right parts of the top diagram are separate diagrams in the original paper, where the left one is an object diagram and the right is about mechanism. The mechanism diagram incorporates some of the same elements from the object diagram. This incorporation creates a visual consistency between them, which contextualises the molecular alignments in the mechanism of interaction. Thus it can be easy for the viewer to quickly understand the roles of the molecules both *in situ* and within the multi-dimensional interactions.

Figure 4.2.7.23B employs very similar elements to Figure 4.2.7.23A for representing similar meanings: protein-gene binding and separation. This diagram combines the drawings with a table, which contains activities and events explained by the drawings. There is a blank space between the drawings and the table, yet the table is arranged in line with the corresponding drawings. Each drawing in one row explains one phenomenon in a row of the table, so these two separate visual items are actually correlated. The upper part (the linear genetic pathway) explains the positive relation of gene *egl-1* to apoptosis. In the original paper, these two diagrams are adjacent to each other as seen here. This arrangement associates two pieces of information: (a) the upstream regulation of *egl-1* by the protein-gene binding, which is represented by the drawings, and (b) the relation between *egl-1* activation and cell death, which is represented by the linear pathway. This association helps the viewer understand the table. To sum up Figure 4.2.7.23, Figure 4.2.7.23A exemplifies how visual elements can “travel” as modules for creating visual consistency, and Figure 4.2.7.23B shows how seemingly separate visual items join to create a coherent explanation for a phenomenon. Note that the information represented by these joint visual items is heterogeneous. Section 5.5 will elaborate on the heterogeneity in mechanism diagrams.

Figure 4.2.7.24 presents three diagrams of membrane receptor-involving mechanisms. These are object-centred mechanism diagrams, too. In all of them, the receptors and their adaptor proteins (such as TRADD and FADD) are (1) the largest icons and (2) centrally located. These diagrams also have other features in common. Firstly, all three papers concern the same receptor family and protease that act with this family, ie. receptors for TNF (tumour necrosis factors) and the protease MACH. Secondly, all three diagrams somehow resemble the biological structures. Although the tertiary structures of the proteins are simplified when depicted in two dimensions, these diagrams provide the important conformational formation about the subunits. Thirdly, while these three diagrams concern slightly different subunits of the receptor-adaptor complex, they all represent the relevant units of the complex with basic graphs. Finally, as a result of the emphasis on protein complex structure, other components in the mechanisms are represented by basic elements, such as

words and arrows. Only the structures of protein complexes are depicted in detail. The cell membranes in these three diagrams are represented by very basic visual elements, serving as the background location of the receptors. The informed viewer does not really need a sophisticated icon for the cell membrane because the membrane location of TNF receptor family is common background knowledge. In such object-oriented mechanism diagrams, the objects are much emphasised than in Figure 4.2.7.23. Even though the viewer has limited background knowledge, they can recognise the centrality of the protein complexes in these mechanisms and appreciate the roles of these structural parts. The growing knowledge in receptor structures and their functional parts may have contributed to such a visual emphasis on the structural details. These diagrams are from the late-1990s to 2000, when the era witnessed the explosion of data of protein structure determination.

A more important implication of the examples in Figure 4.2.7.24 is that mechanism diagrams integrate different perspectives, scales, and interests. When the viewer's eye moves from the receptors downward, it finds that the indicative arrows previously pointing to the subunits are transformed and become causal arrows leading to the activation of downstream proteins and apoptosis. The indicative arrows and the causal arrows are visually very similar. Figure 4.2.7.24B does not have such a transition of the functions of arrows, but it too shows a transition from object-depiction to the description of cellular events occurring in another space at another time. This is to say that different *perspectives* are represented in the same diagrams. The time scales are also different between different parts of the diagrams, for the downstream activations and the completion of apoptosis take places through different time courses. Last but not least, the interest in static entities and the interest in dynamic processes co-exist in these diagrams. The upper (also the major) parts of these three diagrams capture the appearances of receptor structures in a static manner, while the lower parts display a dynamics triggered by the receptor complexes. The ligand-receptor bindings reinforce the integration of the static and dynamic parts. In Figure 4.2.7.24A, the binding is visually vague, for the diagram only points out the binding site on the receptor. In Figure 4.2.7.24B, the binding is drawn in a relatively static way, where the picture shows a complex that is already formed. In Figure 4.2.7.24C, the bindings are visually dynamic because of the arrows. These three diagrams have different ways of depicting ligand-receptor bindings in their object-oriented compositions. But they all build causal relationships between the complexes and the cell events. To sum up the implication of Figure 4.2.7.24, these three examples are visual embodiments of both (1) novel perspectives (eg. protein structure determination) in biological sciences and (2) an integration of different perspectives.

Figure 4.2.7.25 has a typical composition of mechanism diagrams. Instead of emphasising a main object, it equally visualises the component entities of a mechanism. Also, it does not contain a transition of meanings of the arrows. Its somewhat extravagant style probably results from the advancement of graphic tools at that time. Almost every component entity and activity in this cell model has its own representational element. The release of cytochrome c from mitochondria is vividly depicted by the small particles “dropping out” of the mitochondria. The internal layer structure (cisternae) of the mitochondria is depicted in an artistic way. Apoptosome is a multi-molecular protein including cytochrome c and Apaf-1, functioning to activate procaspase-9. In this diagram, the icon of apoptosome is composed by nicely gathering the icons of member proteins in the form resembling the top view of the structure of apoptosome. This 2005 diagram integrates *at least* the following research perspectives:

1. the sectional view of mitochondria, revealed by electron microscopy earlier in the mid-twentieth century;
2. the top view of apoptosome structure, which is as novel as most of the protein structures discovered since the very late 1990s;

3. the biochemical causal links between the cell events;
4. different time scales of the events.

Section 5.5 to 5.6 will discuss the visual integration of heterogeneous perspectives in mechanism research.

Considering Figure 4.2.7.24 and Figure 4.2.7.25 together, it is suggested that the growing complexity of ideas about mechanisms from the 1990s can result in very different ways of configuring diagrams. Advanced graphic technologies can have influences on the style, but not always. Novel elements and styles are created, while traditional compositions are still in use. The multiplicity of visual elements is from the coexistence of old and new ones. Section 5.4.2 will explore the complicated relationship between technological development and visual evolution of mechanism diagrams.

Figure 4.2.7.26—as a mechanism diagram—has a strikingly different feature compared to the others: its lack of causal arrows. The only use of arrows in this case is to indicate the directions of molecular interactions. The original caption is attached here, showing that this is clearly a mechanism diagram. This diagram contains four depictions of apoptosome (Part B to D). Part A is an object diagram showing procaspase-9 binding to its inhibitor. The four depictions of apoptosome-caspase-9 complexes are highly simplified and composed of basic graphics. For example, the apoptosome is given a dish-like appearance. These four depictions could be viewed as separate object diagrams, if the viewer does not refer to these three sets of components: the word boxes above each of them, the word labels of scenarios I and II, and the caption. Without these components, the four depictions are merely about the static structure of apoptosome. But the three sets of components correlate the four depictions with each other. The labels of the scenarios indicate that there are two possible directions for downstream reactions. The word boxes and the caption show the sequential and causal relations between the left two and the right two apoptosome-caspase-9 complexes. Thus the four depictions are cross-associated from top to bottom and from left to right. In this sense, Figure 4.2.7.26 is a mechanism diagram without an explicit visual vocabulary that points out the causalities (the conditions for caspase-9 activation), while it does visualise the prediction of activities (the two scenarios for caspase-9 activation in either way). The ribbon structure of the binding between procaspase-9 and its inhibitor provides supplemental information. The intentional consistency in colour between the ribbons and the schematic depictions of caspase-9 correlates the actual conformational structure with the simplified depictions. In conclusion, Figure 4.2.7.26 is a very rare and special case in the large population of diagrams surveyed by this thesis. Despite its lack of explicit causal vocabulary, this 2004 diagram also embeds the growing complexity of ideas and the multiplicity of perspectives in apoptosis research, just like most of the cases since the mid-1990s,

Figure 4.2.7.27 (2000) serves as a straightforward example of accommodating the growing complexity of ideas through synthesising various and multiple elements. It is straightforward in the sense that the viewer does not need to decipher its visual language to recognise those heterogeneous perspectives. Each different packet of information is represented separately by different iconographic elements, where different perspectives are embedded. Two kinds of basic graphics (ellipses and squares) stand for proteins and protein-related events respectively. By adding a three-dimensional effect, these two icons are turned into the icons of two membrane receptors. Chemical formulae are simplified and modified, so the details are not distracting. Only the phosphate symbols (P) remain unmodified, so it is clear when and where the phosphorylation process takes place. The extracellular matrix (ECM) is also represented by basic shapes with a three-dimensional effect, with the straight lines resembling the actual appearance of ECM. The arrows have two forms: the bold ones indicate molecular interactions, and the thin ones indicate the directions of downstream

phenomena (such as “proliferation” and “survival”). Finally, the cell membrane is represented by an arch, which is also imposed a three-dimensional effect. Such an effect creates a visual illusion that the overall reaction progresses toward the lower right part and the near end (from the viewer's point). This cell membrane icon functions more than indicating the location of the membrane. It directs the viewer's eye along the direction of the reactions. Moreover, it adds an aesthetic value that is more than decoration, for it suggests a *dynamics*, and dynamics is essential in all kinds of mechanisms. The overall arrangement of the elements follows the same visual *syntax* of representing a dynamics: elements at the far end are small, and elements near the viewer's point are large. This arrangement works with the cell membrane icon to create a feeling of multiple dimensionality.

Here is a summary of the multiple perspectives synthesised in Figure 4.2.7.27: the simplified chemical structure, the resemblances to ECM and receptors, the entirely symbolised proteins, and the arrows representing both interactions in space and processes through time. These are visualisations of information from various sources. The information is *heterogeneous*. Such heterogeneity is seen in so many examples of typical mechanism diagrams that one easily takes it for granted. This diagram nicely employs multiple representational resources and demonstrates that the component information of a mechanism must be obtained from diverse practices.

Such multi-perspectivity is exemplified in Figure 4.2.7.28 by creative merging two experimental photographs, a graph of experimental measurement (without number), and a schematic model. The whole diagram can be compared with Figure 4.2.6.29 from *Cancer Research*, for both of them integrate data images and mechanistic models in an inter-referencing way. In Figure 4.2.7.28, this way especially generates dialogues between observation and explanation, and theory and prediction. As Chapter Two has introduced, such dialogues are the crucial part of continually developing and modifying mechanistic explanations. Below I review the details of this diagram to show how inter-referencing happens.

The fluorescence photograph in Figure 4.2.7.28A demonstrates a reciprocal relationship between the levels (ie. concentrations) of two proteins at different maturation stages of the germline in a nematode (*C. elegans*). The two proteins are stained with fluorescent dyes, where CEP-1/p53 is green and GLD-1 is red. CEP-1/p53 plays a role in DNA damage-related cell death. Because GLD-1 represses translation of CEP-1/p53, mutation of the gene for GLD-1 (*gld-1*: a gene coding a specific protein is the protein's name put in lower case alphanumeric characters) de-represses this inhibition and indirectly enhances the cell death rate. The mutual changes of expression level between CEP-1/p53 and GLD-1 are illustrated in the upper part of Figure 4.2.7.28B. This chart graph does not have the actual measurements and shows the reciprocal relationship that is partly quantitative and partly qualitative. The horizontal axis represents the progressive maturation, and the vertical axis represents the level of protein expression, which is determined from fluorescent intensity. There is a serial transformation of ideas between Figure 4.2.7.28A and the chart graph—from visualisation of proteins to quantified intensity of fluorescence, then to chart plotting. Moreover, the germline in the photograph and the maturation stages in the chart are “roughly aligned” (Schumacher et al. 2003) with each other. This alignment creates an inter-reference relationship between these two images. Compared to Figure 4.2.6.29, Figure 4.2.7.28 engages the viewer in a more active inter-referencing process. In Figure 4.2.7.28, the photograph visualises the fluorescence levels as displayed in the chart, and the chart displays the meanings of different degrees of fluorescent intensity. The green words (“apoptotic zone”) and lines underneath the right half of the chart stand for a range of timings, when CEP-1/p53 is released from inhibition because of the falling level of GLD-1.

Adjacent to the chart, there is a schematic mechanism model composed of basic elements. The composition is not complicated because the key message is relatively simple, namely the inhibition

and expression of CEP-1/p53 under conditions with and without GLD-1 in two maturation stages of the organism. This model functions to explain the phenomenon visualised in the photograph in Figure 4.2.7.28 C. The blue-colour DAPI fluorescent dye stains cell nuclei. In an apoptotic cell, the chromosome condensates and the nucleus shrinks. Thus the obviously smaller and condensed blue stains are the indices to the locations of apoptotic cells. This photograph (Figure 4.2.7.28C) shows an increase of apoptosis in certain regions of the two individuals. These individuals are *gld-1* mutant and have a higher expression of CEP-1/p53. Consequently, they exhibit higher cell death rates. The underlying mechanism is explained by the schematic model in the lower part of Figure 4.2.7.28B. These regions contain cells in the stages of activation of CEP-1/p53, which is shown in both the chart graph and the photograph in Figure 4.2.7.28A.

Here is a summary of the importance of Figure 4.2.7.28. Its coherent arrangement embodies a consistent process of transforming and translating ideas during the practice. This arrangement creates an inter-referencing relationship between each part of the diagram, where different parts represent different perspectives for the same set of phenomena. This case exemplifies the richness of mechanism diagrams. Section 5.5.3 will explore the meanings of such inter-referencing arrangements.

Figure 4.2.7.29 is impressively metaphorical yet very effective in communicating the mechanistic idea. It also represents how apoptosis researchers (at least some of them) consider cell phenomena from a truly mechanistic point of view. This set of gear wheels is an illustration of mechanical setting. The meshing between the gears is *workable* in the context of mechanical engineering. The arrangement of the two forces (represented by two kinds of arrows meaning “push” and “stop”) matches the directions of a reasonable set of gear rotations. This mechanical setting follows the rules of simple machines and *works*. This diagram is a representation of the cell machinery of life and death, as well as balance and regulation. The red gear stands for apoptotic propensity, and the green stands for proliferation. The grey morphogen gear acts to trigger the rotation of the proliferation gear, while stopping the apoptosis gear. Other factors that may either trigger or stop the gears, such as mitogens and survival factors, are represented by basic visual elements. The directions of these arrows also follow the rules of a workable simple machine.

The scientific message of this diagram is that, in a normal condition, proliferation and apoptosis are *coupled*. Disconnection of this coupling leads to reduced apoptosis and uncontrolled proliferation and eventually diseases, such as cancer. These two propensities are connected by modulating factors (morphogens), which regulate the coupling ratio “in a graded fashion.”<sup>80</sup> Therefore, the gear teeth also have a meaning, as they signal that any potential regulatory response will be grade-dependent on the stimuli (eg. particular survival factors). The original caption uses metaphorical rhetoric, too. It refers to an imagined power that serves as the tension of system and holds the cell machinery stable. This is a diagram of mechanism not only because of the dynamics it conveys but also due to its accurate analogy to a workable machine. This biological diagram is readable and reasonable in the context of visual language of engineering. It also demonstrates that diagrams are useful in communicating mechanical ideas and generating mechanistic ideas with least propositions. Last but not least, this diagram shows the playfulness in expert communication. Examples of other playful trials are also seen in the use of non-specialist elements (eg. scissors) in the other journals surveyed. The original caption of this diagram confirms the author's “playing”: “I am grateful to my colleague, Michael White, for inspirational discussions and to his son, Alex, for use of his toys.”<sup>81</sup>

Such playfulness appears again in Figure 4.2.7.30. Figure 4.2.7.30A is from *Cell*, and 4.2.7.30B is from *Cancer Research* (already cited in Figure 4.2.6.35). Both diagrams use emoticons for representing the dying cells. As mentioned in Section 4.2.6, this use adds a “personality” to the

<sup>80</sup> Abrams, 2002, 405, Figure 1.

<sup>81</sup> Ibid.



dying cells and animates the apoptotic process by showing the progressive “emotional” changes. The *Cancer Research* diagram (1999) is published before the *Cell* diagram (2003), but it is unclear whether the latter was inspired by the former or this visual similarity is coincidental. The point of this case is that the metaphorical associations between life and happy emoticons and between death and sad emoticons are both intuitive. Thus it should not be surprising if these two cartoons of “emotional progress” coincidentally echo with each other.

Figure 4.2.7.31 is a rare case of mechanism diagram. This is almost a gathering of chemical structure diagrams. A similar case is seen in *Cancer Research* (Figure 4.2.6.27), but this *Cell* diagram has even fewer narrating elements normally found in mechanism diagrams. Unlike Figure 4.2.6.27, no other information (such as biological events) than chemistry is shown. This diagram is about caspase-3, a crucial enzyme in apoptosis. Apart from the chemical formulae, this diagram contains some arrows respectively pointing out (1) the structural changes (from *a* to *d*) and (2) the interactions between the amino acids within the enzyme, where (2) leads to (1). The message is that the enzymatic activity of caspase-3 is formed by the overall structural changes, which result from sequential interactions (eg. removal or addition of protons) between the constituent amino acids. In other words, the small arrows explain the changes indicated by the large arrows. The causal relationships are not explicit due to such a subtle form of expression. This diagram can be viewed as a representation of mechanism only under two conditions. Firstly, sufficient background knowledge is provided partly by the text. Secondly, when this diagram is appreciated in the sense of “biochemical mechanism”, such as a transformation of chemicals involving transfer of protons or other acid-base reactions.

The three diagrams in Figure 4.2.7.32 exemplify two points: (1) the persistent use of basic and traditional styles and (2) the possibility to show creativity with basic and traditional styles. These three diagrams are published in 1998 (A), 2003 (B), and 1994 (C). Apart from their difference in image quality, they use nearly the same visual elements. For example, both Figure 4.2.7.32A and 4.2.7.32B contain question marks. These three diagrams on the one hand show that, while knowledge becomes more complex, complex biological mechanisms always contain simple and linear pathways. Therefore, basic configurations cannot be abandoned. On the other hand, these diagrams show that complex perspectives can still be represented by simple elements. For example, all these kinds of information are represented by words in 4.2.7.32C: treatment or an affecting factor (radiation), genetic substance (p53), and cell events (eg. cell cycle arrest). Most of the cases surveyed suggest that the increase of complex ideas tends to parallel a growth of complexity in visual representation, but this case provides a counterexample.

In some cases of using simple elements and basic styles for representing complicated ideas, creativity acts as the key to effective communication. However, as shown by some previous examples, visual experiments can cause confusion. Figure 4.2.7.32A employs slightly different arrows to represent different things. The bold one between *ced-1/ced-7* and *ced-6* genes means a downstream relation of *ced-6* to the other two genes. The small and repeated arrows mean the suppression of engulfment defect, ie. the promotion of engulfment (the two arrows signifying a double negative). These arrows themselves are not obscure, but the arrangement of the symbols for the genes and the engulfment makes the pathway not easy to follow. The *ced-10* symbol with the question mark means something undetermined, but its exact meaning in this model is hard to interpret. The location of words “*ced-2*” and “*ced-5*” triggers confusion, for the words are not associated with any other components of the model. It can only be speculated from reading the original caption that these two genes possibly act either in parallel with or downstream to *ced-6*. In sum, the components of this diagram are too scattered to construct a coherent narrative. Understanding this diagram requires a lot from reading the text. By way of contrast, Figure 4.2.7.32B—composed of the same elements—is more independent from the text, for its composition is

able to coherently narrate the mechanism.

Figure 4.2.7.32C shows creativity in a subtle and interesting way. This diagram contains elements as simple as the other two, but it curves some of the arrows to create a new meaning, ie. the radiation treatment. Such an “economic” use of visual elements surprisingly renders a lively depiction of the concept, where the curvy arrows resemble a commonplace imagination about radiation rays. The separation between the three parts of this diagram is not confusing, since each part is labelled with descriptive symbols for the conditions. The consistency of visual elements and their forms makes these three conditions parallel and comparable to one another. The blank space simultaneously separates and correlates the conditions. Such a use of white space can be considered in the art history context: it is similar to the whiteness between *Encyclopedia* tableaux that Bender and Marrinan discuss (2010; see Section 2.5.1 of this thesis). Namely, this space informs the viewer that these parts are separate scenarios and should be cross-referenced in a coherent manner of interpretation.

#### 4.2.8 FASEB

Figure 4.2.8.1 presents the data profile of *The Journal of the Federation of American Societies for Experimental Biology* (abbreviated as *FASEB* hereafter). The earliest issues available from the archive date from 1987, but only four apoptosis papers in the 1980s were returned by search. Just like the previous journals, apoptosis papers in *FASEB* drastically increased since the 1990s. Search results were sampled with the methods described earlier and at a quite low confidence interval (less than 6). Figure 4.2.8.2 shows the profile of samples.

Figure 4.2.8.3 presents the changes of D/VI. From 1990 to 2005, the D/VI decreases from around 0.18 to 0.12, where the rate of decrease is 30.33%. Such a decrease appears different from most of the journals surveyed, as the others generally tend to have increasing coverage of diagrams.

Figure 4.2.8.4 shows the frequencies of two prevalent diagram types (object and mechanism) in the 1990s and 2000s. When the object type remains almost the same (1990s: 0.0176; 2000s: 0.0181), the mechanism type decreases from 0.15 to 0.09. The implication of these results is a decrease of employing mechanism diagrams in visual communication. This contrasts *FASEB* to most of the journals surveyed<sup>82</sup>. The authors' interest in diagrams both in general and of mechanisms appears to decline.

Nonetheless, a further investigation of the proportions of the five diagram types suggests another scenario. Figure 4.2.8.5 makes longitudinal and horizontal comparisons between diagram types. The mechanism type is the only prevalent type that persists, while the other types either stay unchanged or increase without becoming prevalent. The mechanism type decreases in proportion at a relatively low rate. Meanwhile, Figure 4.2.8.6 shows that there is an increase of all types of diagrams in the 2000s. The results from calculating the frequencies (D/VI) of different types (Figure 4.2.8.8) show that *FASEB* does not really shift its focus of interest from mechanism to the other types in the 2000s. This suggests that some kind of visual items takes over the coverage, displacing mechanism diagrams with non-diagram images. Then what is this kind?

The answer may be found in Figure 4.2.8.7. In 2000, *FASEB* launched a new category of articles “*FJ Express*” (*FASEB Journal Express*). Articles in this category are generally in the form of typical

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<sup>82</sup> Five out of eight journals surveyed show increased frequencies of mechanism diagrams from the 1990s to 2000s. Apart from *FASEB*, the remaining two had not been founded until 1999.

research papers, but they are special due to the “express” feature. The editorial addresses that this *Express* category “...is a new approach to the rapid publication of research communications”<sup>83</sup>. Accepted articles in this category are published online with digital object identifiers (*doi* numbers) and without page number before they are printed. There seems to be no fixed instruction for image editing in this category, but a lower D/VI of this category is notable. The overall D/VI of the journal in the 2000s is 0.12, where the D/VI of this *Express* category is only 0.05. All the other categories are higher in D/VI: *Research Communications* (original papers) has 0.09, *Reviews* has 0.88, and *Hypothesis* has 0.89. That is, in 2000, *FASEB* introduced a new category of papers containing considerably fewer diagrams compared to the other categories. This new, online-first category aims to publicise novel findings sooner than traditional channels. Figure 4.2.8.7 displays how the emergence of *Express* papers changes the relative proportions of paper categories. This *Express* category is a data-heavy one and focuses on data images rather than diagrams.

Here I get back to the comparison between the decrease and the increase of different diagram types from 1990 to 2005. To find out the reason for the decreased coverage of diagrams in general, the weighted contribution of each different type to the overall rate of decrease is calculated. Figure 4.2.8.8 shows the changes of D/VI of all five types. Table 4.1 lists below the contribution of each type to the change of overall D/VI:

**Table 4.1 Rates of D/VIs decrease in *FASEB***

	diagram/VI	object/VI	CS/VI	ED/VI	mechanism/ VI	other/VI
'90-'99	0.177	0.02	0.004	0.003	0.153	0.000
'00-'05	0.123	0.018	0.003	0.005	0.095	0.001
rate* of decrease	30.326	-2.293	-19.480	103.901	38.075	N/A
proportion	1.000	0.100	0.020	0.015	0.865	0.000
weighted** rate of decrease		-0.229	-0.056	0.563	32.931	N/A <sup>#</sup>

CS: chemical structure

ED: experimental design

\* Rate as %

\*\* multiplying the rate of decrease by proportion

# divisor = 0

Amongst all five types, the fallen frequency of the mechanism type is most influential (32.93%) to the decrease of overall D/VI. This results from (1) its large decrease of frequency (38.98%) and (2) its prevalence in proportion (86.5%). The ED type even shows a greater decrease (103.9%), but it is less influential due to its low proportion (1.5%). The other types, no matter they increase or

<sup>83</sup> FASEB, 2015.

decrease, are too low in proportion to have much impact on the overall D/VI.

In conclusion, a decrease of mechanism diagrams is the main reason for the general decrease of coverage of diagrams. The new *Express* category is designed for rapid publication of data. While this category also employs diagrams of all types, it does not have an obvious interest in contextualising the discoveries in big pictures. This is reflected in its visual culture: the low D/VI of mechanism diagrams.

*FASEB* falls in the group of relatively high D/VI in all the journals surveyed (Figure 5.1). That is, from the 1990s to the 2000s, diagrams remain a relatively important means of visual communication in *FASEB*. The mechanism type remains dominant, but it indeed loses part of its coverage to the data images in the *Express* category. The analysis of image contents in the *Express* category shows that this category prefers images that are (1) less-transformed from first-hand laboratory data and (2) very specific to the topics. Perhaps this growth of coverage of data images can be considered as reflective of this journal's response to the atmosphere of biological research in the new century—increasingly competitive in publishing novel findings and diverse (and thus specific) in research interests.

From this paragraph onwards, I present the qualitative results. The majority of object diagrams are representations of macromolecular structures in simple styles. This is the same with the other journals. No peculiar style is found. Other themes (eg. drawings of other entities) appear at very low frequencies. Figure 4.2.8.9 presents two examples of non-macromolecule object diagrams. Figure 4.2.8.9A is an experimental apparatus, and Figure 4.2.8.9B displays the interrelationship between two kinds of cells and blood vessels (N: neuron; A: astrocyte, or glial cell in earlier neuroscience literature; V: blood vessel) in the brain during development and in noxious situations. The serial drawings in 4.2.8.9B do not have a sequential order but represent the interrelationships between the cell kinds in different conditions. Note that this diagram is, according to the author, a representation of “speculative interaction” between the cell kinds. The key message is about different loci of aquaporin-4 expression on the cells, so this is an object diagram. Nevertheless, it is also arguable that this diagram can be considered as a quasi-mechanism diagram due to its implicit suggestion of the mechanisms induced by the protein expression and the intercellular spatial relationships. It is not a mechanism diagram, for it lacks an explicit narrative of process and causality.

The chemical structure type has a very low frequency. All the samples are about artificial reagents used to treat cells in experiments.

The experimental design type is also minor, where most of the samples are graphic representations of biotechnology. The styles found in the ED type vary a lot. Sometimes the style is as simple and linear as Figure 4.2.8.10, comprising of basic elements, such as symbols and arrows. This linear composition concisely conveys the linear process of chemical treatment and sample collection. Sometimes the style is as figurative as Figure 4.2.8.11A. Each entity has its own representational visual element. The intestinal epithelial cells are drawn one by one, and the two micro-electrodes of the conductance probe are clearly depicted. The original caption does not provide the meaning of the circle inserted between the epithelial cells. I suppose this circle to be a neutrophil (a kind of leukocyte), judging by its multi-nuclei and round shape. The message of this diagram is a measurement of electric current across the cell layer. It concerns nothing about the ambiguous round cell.

Figure 4.2.8.11B presents a special case of ED diagram. Its composition and elements are both very simple. The drawing resembles a petri dish used in experiments. The drawing of petri dish is adjacent to the photograph series of experimental results. The petri dish is used to grow genetically-transformed derivatives of yeast. The four divided areas are used for four different conditioned treatments on the yeast. Such a combination of diagram and experimental images can be compared

to some examples of integrating diagrams and data images found in other journals. The most similar (nearly the same) case is Figure 4.2.2.10, where the drawing shows the design of producing the data image. In a different way, these two petri dish diagrams can also be compared to Figure 4.2.7.16 and 4.2.7.28. They are similar in terms of the inter-referencing between data images and diagrams. Meanwhile, they are different due to their different ways of building the inter-referencing pattern. The messages of Figure 4.2.8.11B and Figure 4.2.2.10 are straightforward. The viewer can easily correlate the experimental design with the results. Such parallel arrangements and the direct visual correspondences make Figure 4.2.8.11B different from the other two complicated cases.

The “other” (miscellaneous) type in *FASEB* is more diverse in content and has more rarities compared to the other journals. Figure 4.2.8.12 is a collection of chemical reactions. In a strict sense, its status of being a diagram is somewhat arbitrary. But it is categorised as a diagram, for it is numbered as one of the figures in the original paper. It is not a representation of static chemical structure, for these formulae represent w dynamic reactions. On the other hand, it is a very traditional kind of visual item, resulting from the standardisation of representing chemistry in the early age of modern science. In scientific journals earlier than the middle twentieth century, when the other four types of diagrams were till underdeveloped, such collections of chemical reactions appeared widely as a kind of visual item other than plain text.

Figure 4.2.8.13 presents a rarity in the form of pie chart, which also has an early origin. But this diagram is beyond the convention of pie chart and requires the viewer's effort to overcome its ambiguity. The visual convention of pie chart is visualising quantitative data by correlating the relative sizes of pieces to the proportions. However, this pie chart does not provide the information about what data is represented. Nor does it provide the scale of quantity. Most of the words labelling the pie pieces are names of genes involved in some cell events (apoptosis, cell cycle, differentiation and related reactions). Meanwhile, there is a piece labelled as “apoptosis”, which is not a gene's name. The original paper conducts an experiment to investigate the expression of these genes under the treatment of a reagent named imatinib. In the original paper, supplemental data to this diagram is in a separate table, which lists the results of quantifying the expression of these genes. The results are the ratios of gene expressions to the control group. They suggest that some of the gene expressions are reduced by the treatment and some are increased. The separate table explains the difference between the pie pieces, but it leaves no answer to two curiosities: what the “apoptosis” piece is and what the colour spectrum means. The diagram itself describes the meanings of some colours, but this leads to further ambiguity of the remaining details of the spectrum. The viewer needs to refer to the table and associate the ratios with the different colours so that the spectrum becomes meaningful—the different colours represent different extents of “increased expression” from high to low in a clockwise manner. But still, no description is given to the existence of the “apoptosis” piece. This piece appears to be a check point between increase and decrease of gene expression. Also, it is not explained how the piece sizes are determined. Finally, the arrangement of the different sizes does not really correspond to the table.

To sum up Figure 4.2.8.13, the function of this diagram in the whole argument (the paper) is unclear. This diagram indeed conveys the idea about the (roughly) two groups of genes expressing differently under the treatment, but this conveyance is not as effective as the table. If it is to offer a feeling of the relative expressions between the genes, the visual language does not help much. As shown in previous sections, ambiguous and creative styles are like visual experiments. However, experiments may sometimes fail to perform desired effects.

Branching compositions (such as Figure 4.2.8.14) have been seen in the other journals. Figure 4.2.8.14 displays a family of heat shock transcription factors (HSF) in different species of higher eukaryotic organisms. The numbers represent the extents of identity (in percentage) between the branches. Branching compositions are good at representing a group of phenomena and entities that

have a “branching-out” relationship in terms of structure or reaction.

Figure 4.2.8.15 is similar to Figure 4.2.8.13 in the sense of borrowing a style from existing kinds of graphs and employing the conventional visual language. They are also similar for their lack of quantitative information. But Figure 4.2.8.15 requires less effort to interpret, without the need to refer to supplemental information. The message can be quickly read. In pre-diabetic condition, insulin production meets insulin requirement. The failure of insulin production to respond to insulin requirement is followed by the onset of diabetes. This diagram is from a review paper, so it is likely that the purpose of such a schematic representation is to convey very general concepts but not complicated ideas. In the original paper, experimental results are given next to this diagram, while they are not directly correlated to each other. The results show a lipid accumulation and the enlargement of the islet cells for compensating the pre-disease phase. Then the cells decline drastically. These results are the indicators of pathophysiological changes during prediabetes and diabetes. In sum, this diagram can be viewed as a model made by extracting and transforming these ideas from the experimental results: (1) insulin requirement raises due to lipid accumulation in obese, and (2) insulin production decreases (which is confirmed by cell morphological decline). This diagram does not need quantitative details to clearly convey the mismatching between insulin requirement and production or the relationship between this mismatching and disease development.

The mechanism diagrams in *FASEB* do not have typical styles. Most of the cases have simple elements and compositions, where the styles are varied. Below I discuss some creative (but not anomalous) examples.

Figure 4.2.8.16 presents two cases of depicting mechanisms in somehow overly detailed ways, where the details can be simultaneously distracting and helpful to animating the mechanisms. Figure 4.2.8.16A shows the roles of RB1 gene in two different apoptosis-involving conditions: retinal cell differentiation and erythropoiesis (red blood cell production). Without RB1, retinal cells proliferate in an uncontrolled manner. Such proliferation results in malignancy and apoptosis of red blood cells. In the upper panel, the gathering of the increasing cells represents tumour. In the lower panel, the icons of decreased and morphologically changed cells represent dying blood cells. But such detailed drawings do not necessarily convey relevant messages. For example, the numbers of the cells could be fewer, and the morphological change could be represented by other simple elements (eg. words). However, such a seemingly redundant use of elements can help the viewer mentally animate the mechanisms.

Similarly, Figure 4.2.8.16B contains drawings of a lot of cells to represent cancer development. Along the development process, the icons of cells and the blood vessels both increase, and the icons of blood vessels become bigger and more branched. The latter represents angiogenesis of the tumour. Even the symbol “angiogenesis” gradually becomes bigger from the dysplasia stage (when cancer remains at the original site) to the cancer metastasis stage (when cancer starts to invade around). Some details are not really relevant, but they are also drawn in detail, eg. the schematic and symbolic basement membrane. This is possibly to provide a background for displaying the spatial relationships between the cancer cells, the blood vessels, and the structure of the original site. The key message of this diagram is the preventive and interfering roles of antiangiogenic agents in the progression of tumourigenesis. This message is put at the bottom of the diagram, where the arrows indicate the interfering actions. The arrows are put in a relatively lighter colour than the other drawings. In conclusion, the cartoons in this diagram can also trigger a vivid imagination about cancer progression, though many of the artistic details are not scientifically relevant. For example, the details of cancer progression (such as the increase of cells and the expansion of blood vessels) are not the key message. Therefore, similar to Figure 4.2.8.16A, such an extravagant use of elements may at the same time distract the viewer from the key message while mentally animating the mechanism.

Figure 4.2.8.17 (2005) shows the influence of advanced graphic technologies in the middle 2000s, while the extravagant details can be as distracting as the above two cases. The employment of new graphic tools is embodied in many components, such as the three-dimensional depiction of cells, the colour gradation of both the background and the arrows, and the complicated colour filling of the Kupffer cells (KC). Similar to Figure 4.2.8.16, this diagram offers vivid and colourful animation of the mechanism. The flesh-like colour of the hepatic stellate cells (HSC) nicely represents the biological feature of the environment. The enlargement of icons of HSC, which represents liver fibrosis, and the morphological change of KC nuclei from round wholes to small particles represent the nuclear change in apoptosis. Nonetheless, advancement and sophistication of graphic technology do not necessarily synchronise with development of composing skills and sophistication of styles. If these aesthetic decorations are removed, both the composition and the narrating style of this diagram are found basic. The key message of this diagram is about the role of a reagent, SC-236, in attenuating liver fibrosis via reducing the release (or down-regulating the activities) of certain inflammatory substances. Thus this key message is concentrated in the right part of this diagram, which only contains basic elements (symbols, arrows, and a square) and simple colours. The visually attractive components (such as the KCs and the HSCs) merely display the background environment for the actions of SC-236. This diagram is from the same paper with Figure 4.2.8.10. The experiments of the paper are to test the functions of SC-236 but not investigate the pathology of liver fibrosis. The pathological changes in liver fibrosis are the background knowledge, but they are visualised by more extravagant elements than the key results. This diagram conveys the key message without ambiguity, but the unbalance in its visual emphasis between the key message and the background can be misleading.

The dominance of chemistry contents in Figure 4.2.8.18 appears to be similar to some previous cases that contain mainly chemical formulae and reactions, such as Figure 4.2.7.31, Figure 4.2.6.26, and 4.2.6.27. This diagram is categorised as the mechanism type for a similar reason. Although the symbols indicating “free radical oxidation” and “rearrangement” are less noticeable than the reactions, they work with the indicative arrows of structural changes to represent a gathering of pathways. These pathways contain causes and effects. The series of four chemical compounds are represented by symbols that are not standard visual language of chemistry (“4 H<sub>2</sub>-IsoP regioisomers”). Yet such a style is somehow too idiosyncratic to make this diagram a typical mechanism diagram. To sum up, this is a quasi-chemical structure diagram composed of mixed visual languages, and the causalities make it a mechanism diagram at the same time.

Figure 4.2.8.19 includes a mechanism diagram (4.2.8.19A) and a diagram of the “other” type (4.2.8.19B). The most impressive feature they have in common is the concentric structure composed of multiple layers. In Figure 4.2.8.19A, the arrows bridge the triangular layers. In Figure 4.2.8.19B, no visual element links the circular layers. This is the major difference that differentiates them.

The core of Figure 4.2.8.19A represents the cell redox status, which involves the redox carriers displayed in the fourth (the most inner) layer. This status is to be coupled with specific genes expressed by the agents in the third layer. Genes in the second layer regulate the cell events listed at the bottom of the diagram. Compounds in the first layer act at the checkpoints, mediating cellular processes modulated by the factors listed on the top of the diagram. The modulating factors are located outside the triangles because they act upon the cell from the external environment. Their actions eventually cause the cascades of signalling pathways inside the cell. The arrows are too simple to explicitly narrate all these interactions, but the interrelationships amongst different layers can be told through careful interpretation based on background knowledge. It is unclear whether or not the author intends to suggest any hierarchical relationship between the layers. But it is clear that the closer to the core a layer is, the later it gets involved in the signalling cascades.

This creative diagram has weakness in visual communication, though. The weakness results from the inconsistency of its visual language. The white arrows that link all the layers do not have the same meaning. Sometimes they mean “coupling”, and sometimes “regulation”. The classification of the substances in each layer is vague. This diagram lacks a coherent logic of its visual language (ie. elements and composition, or visual vocabulary and syntax). This makes it somehow difficult to interpret the meanings. On the one hand, this diagram conveys the idea of a cell model, for it draws a boundary of the system. The message is clear that the input factors (symbols above the system) cause the consequences (symbols beneath the system) via specific reactions within the system. But the details of the model need to be understood along with the text. The text maintains that these details, but not the layer structure, are actually the key message of this diagram. As previously shown, visual experiments can be intriguing and obscure at the same time.

Figure 4.2.8.19B has a layered structure similar to Figure 4.2.8.19A. However, this set of concentric circles is not accompanied by any supplemental element. While such a minimal use of elements avoids the problem of logical inconsistency that Figure 4.2.8.19A has, it also obscures the message. This diagram is merely a display of a very basic biological concept: the hierarchies of biological systems. A diagram in a research paper should convey more. According to the original caption, the diagram really is about the common-sense concept of the hierarchies from group to individual levels and from macro to micro scales. The original paper is a review paper on studies of longevity. It covers both environmental factors (the macro-scale) and molecular mechanisms. Thus this diagram is mainly about the interrelationships between macro- and micro- environments. The smaller circles are subsets of the larger ones. It is almost unlikely to interpret this message without reading the text.

Now I get back to the difference between this diagram and Figure 4.2.8.19A. This diagram belongs to the “other” type. Neither its visual language nor its key message concerns any causal relationship or status change, which are both included in Figure 4.2.8.19A (a mechanism diagram).

Figure 4.2.8.20 to 4.2.8.23 are examples of some special features of mechanism diagrams that seem to be common across the journals surveyed. Figure 4.2.8.20 presents two cases from two decades. Both emphasise the mitochondria and represent the remaining components with very basic elements. Similar cases have been shown in Figure 4.2.6.33 (*Cancer Research*) and Figure 4.2.3.11 (*Cell Death and Differentiation*). Figure 4.2.5.9 to 4.2.5.11 (*Nature Reviews Molecular and Cell Biology*) have shown a noticeable “template” icon of the mitochondria, where the remaining components of the diagrams are composed of very basic graphics, too. It should be noted that these examples are not rare in the journals they are from. Possible explanations include the centrality of the mitochondria in apoptotic mechanisms and the special characteristics of mitochondrial structure. Section 5.3.4 will elaborate on these two explanations.

Figure 4.2.8.21 serves as a case contrast to the above cases of visual emphasis on the mitochondria, for it emphasises a specific entity (brain) for an obvious reason. The remaining components of this diagram are basic graphics, too. In this diagram, only the two brain icons have relatively sophisticated details and resemble the appearance of the brain. The reason for emphasising the brain is that the brain is the location of all the downstream cell events, as the original paper studies the cell mechanisms of seizure. Incorporation of such vivid pictures does not necessarily enrich the scientific content, but it can direct the viewer’s eye to the crucial component entity of the mechanism. This emphasis is different from the above mitochondria cases, where the mitochondria are only a kind of component entities in the mechanisms but not the focus loci.

Figure 4.2.8.22 shows another case contrast to the visual emphasis on the mitochondria. While this diagram has an emphasised mitochondrion, just like the above cases, its emphasis has a reason as obvious as Figure 4.2.8.21. In this mechanism, the mitochondria are the locations of cell events. The molecules are put in various places, both inside the mitochondrion icon and on the outer



membrane of it. Their interactions are also visualised. The key message can be easily appreciated—some molecules go out of the mitochondria to trigger apoptotic reactions. Here, the mitochondrion certainly is the central component entity of the mechanism. An event that is slightly remote from the mitochondria, ie. the activation of caspases, is simply represented by words. This creates a visual distinction between the remote and mitochondria-centring processes.

Figure 4.2.8.23 and Figure 4.2.8.25 both contain visual elements from non-specialist areas. Figure 4.2.8.23 has the icon of scissors, which has appeared in previous journals, such as Figure 4.2.3.14 from *Cell Death and Differentiation*. Here, the scissors also represent an enzymatic cleavage of the substrates (caspase-7 “cuts” the Lyn protein). Figure 4.2.8.25 uses everyday life elements differently. It does not use them as metaphors but really means the actual things. The scissors in Figure 4.2.8.23 do not exist in the enzymatic activity, but over intake of hamburgers (which have an icon in Figure 4.2.8.25) really can cause overnutrition. The viscera icons in the right part of Figure 4.2.8.25 represent real organs. The colouring and the three-dimensional effect of both the hamburger and the viscera vividly resemble the objects. Yellow oil drops are commonplace elements in biological diagrams of fat-related mechanisms. In the right part of this diagram, they represent fat accumulation, where their large sizes (compared to the viscera icons) suggest the large quantity of fat. In the left part, adipocytes (fat cells) are depicted in the same yellow colour. This creates a visual consistency between the fat cells in the left and the fat accumulation phenomenon in the right. The lively use of non-specialist elements makes this diagram potential for engaging a wider audience. Apart from all these everyday elements, the other elements and their colouring in this diagram are quite basic. The stop sign next to the “leptin” symbol is metaphorical, for it means that leptin hormone acts to prevent further lipid accumulation. This diagram is from the same review paper with Figure 4.2.8.25. These two diagrams have similar aesthetic styles, though the other diagrams in the original paper do not. Such a style can facilitate a common goal of review papers: communicating professional ideas through using outsider-friendly language.

Figure 4.2.8.24 includes two rare cases that both have circuit-like compositions. Both are from late-1990s papers. While they both look somewhat ambiguous at first glance, they are different in terms of communicative effectiveness.

Figure 4.2.8.24A displays the interrelationships between different signalling pathways either activated or inhibited by a kind of phospholipid, sphingosine (So) or its metabolite, sphingosine 1-phosphate (SoP). The roles of sphingosine metabolism in cell growth and death are varied, depending upon which pathways it activates or inhibits and what regulatory factors of cell fates are produced in the processes of activation and inhibition. This diagram proposes some “possible sites of cross-talk” (author’s term from the original caption) between these pathways. The upward arrows mean activation, and the downward arrows mean inhibition. The two circular pathways and the rightward arrows next to them (from So to SoP) represent biosynthesis and metabolism of sphingosine. The downstream factors such as PKC and cAMP are important intracellular signalling factors. In sum, this diagram is about a variety of roles of sphingosine in cell signalling. It focuses more on the divergent actions of sphingosine (as well as the material and metabolite of its synthesis) than the interactions between the pathways affected (such as PKC inhibition). The author maintains in the text that the details of those interactions are still unclear. The author draws another diagram (not cited) to display the interactions, but the diagram is merely a list of hypothetical interactions and mainly composed of words. It includes the biosynthesis of sphingosine (partly drawn in Figure 4.2.8.24) and a downstream pathway into the sphingosine signalling, while not really making Figure 4.2.8.24A clearer.

Figure 4.2.8.24A could be drawn in less complicated ways. The “branching” of the bold arrows (ie. the representation of divergent actions) appears as the key message of the diagram. This branching seems to be over-emphasised, so the viewer may quickly notice a group of bold lines taking over

the body of this diagram. The upward and downward arrows are actually crucial to the key message, for they represent the actions of sphingosine. However, they are visually downplayed compared to the bold lines. This diagram resembles an electrical circuit diagram (though it is unclear whether or not this is intended). Such a style is impressively creative and eye-catching yet not necessarily helpful to properly conveying the message. For example, the viewer's eye may have to wander along the lines before locating the true focus of this model.

Seemingly similar to Figure 4.2.8.24A, Figure 4.2.8.24B also configures basic elements in a circuit-like composition. Its composition is even simpler. The arrows look the same or similar, but they have plural meanings. There are four sets of arrows. The first set of arrows is the upper pair of arches. They represent the same route: import of proteins into the cell nucleus through the mediation of nuclear localisation sequence protein (NLS). This route of import is represented by double arrows because: (1) there are two different pathways of activating it; (2) the cell has two separate states, namely resting and activated (these two states are shown by the symbols at the bottom). The lower big circle with a bold outline and four insertions of squares on the outline represents the cell nucleus. The four squares are the pores on the nuclear envelope, where the proteins are imported into the nucleus. The second set of arrows are the three short ones next to both sides of the nuclear envelope in the lower part. They have two meanings: calcium being released out of (right side) and imported into (left side) the nucleus. The third set of arrows is located in the middle to the upper part, linking the calcium ions to two kinds of protein (left: GTP-bound Ran/TC4; right: calcium-bound calmodulin). This set represents “activating a pathway” by correlating the three cellular messengers. The fourth set of arrow is only one arrow, which is the boldest one at the bottom. This arrow points rightwards and indicates the direction of status change.

The visual language of Figure 4.2.8.24B simultaneously represents several complex concepts:

- ⤴ abstract ideas (signalling pathway; import of substances) and the ontology of the entities (nuclear envelope; nuclear pores);
- ⤴ resting and activated states of the cell;
- ⤴ different pathways that act in different states;
- ⤴ different calcium levels inside the nuclear envelope and in cytoplasm.

Although the composition is creative and rare, visual conventions in fact dominate this diagram, such as the “activating” arrows and the “plus” signs (which also mean activating), and the arrows of “import” inserting into the pores. Unlike Figure 4.2.8.24A, the circuit-like composition of this diagram is not difficult to interpret. Both the directions and the endpoints of the paths can be followed according to visual conventions in biology. This diagram exhibits a balance between innovation and convention of style. Besides, the versatile use of arrows surprisingly does not cause ambiguity. Basic graphics tend to have plural meanings in biological diagrams of complex mechanisms. Examples of this convention have appeared in previous sections. Section 5.3.3 will use arrows as a case to discuss the plurality of meanings of basic graphics.

## 4.3 Conclusion

This chapter has presented the results from an empirical survey on apoptosis papers in eight journals through three decades. Each section is dedicated to one journal and structured to present three parts in sequence: quantitative results, qualitative analysis of contents of typical diagrams, and

analysis of contents of rarities.

This chapter has drawn the comprehensive patterns of visual communication in a contemporary biological field. It fills a gap in the existing literature on the relationship between diagrams and practice of biological mechanism research. Due to the novelty of this topic, previous studies tend to investigate relatively small number of cases. For example, Sheredos et al. (2013) proposes to study the relationship between diagrams and mechanism studies<sup>84</sup>. My thesis coincidentally started around the same time, while targeting the more general patterns of a larger population<sup>85</sup>. This chapter complements existing scholarship by building a large dataset. The synchronicity of diagram studies from different aspects can be viewed as an intellectual call for recognising the importance of diagrams in biological mechanism research.

Chapter Five will interpret the results based on the analytical framework described in Chapter Two and Three. Quantitative and qualitative results shall be discussed together. Example diagrams will be compared both longitudinally and across journals.

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<sup>84</sup> This team focuses on circadian rhythms research and has done some case studies on both diagrams and data graphs, eg. Burnston (2015).

<sup>85</sup> This comparison is based on my informal discussions and personal correspondences with the team members. The correspondences have been happening since the Diagrams as Vehicles of Scientific Reasoning Workshop (2015) and the Fifth Biennial Conference of Society for Philosophy of Science in Practice (2015).

## Chapter Five: Discussion

### 5.0 Introduction

This chapter interprets the results (as presented in Chapter Four) and connects the discussions to the existing literature (as reviewed in Chapter Two).

### 5.1 Diagrams: types, frequencies, and trends

This section focuses on interpreting the quantitative results. It will firstly compare my methodology with previous approaches to quantification of scientific images. Secondly, it shall reveal the implications of two major findings: prevalence of two diagram types and their relative changes in coverage.

#### 5.1.1 Introduction to quantification

The quantitative analysis of biological diagrams in this study is inspired by a common perception of contemporary biosciences that visual representations are a crucial part of the arguments. Most of the existing studies on scientific images have chosen a case study approach specifying few examples. Also, the demarcation between different formats of imagery is not always considered. Photographs, graphs, tables, and drawn diagrams tend to be investigated together without distinction<sup>86</sup>. Such a conflation assumes that the different formats are similar or the same in terms of the visual language employed for representation.

Large, quantified studies of scientific images are rare. Gross, Harmon and Reidy (2002) have quantified the coverage of surface area of visual representations in scientific journals published in the twentieth century<sup>87</sup>, showing that visual representations “occupy a sizable proportion of the article's surface area, an average of 26% (18% figures, 8% tables)” (200). The percentage of scientific articles without visual representation dropped from 52% to 12% from the nineteenth to the twentieth century. This change is “dramatic” (200), alongside the steady growth of numbered figures in scientific articles<sup>88</sup>. The authors maintain, “it is impossible to conceive of the argumentative practices in 20-century science without their visual representations (tables and figures).” (2002, 200). This trend affects the structure of scientific argument. The message is obvious: images are part of the argument.

However, Gross, Harmon and Reidy (2002) sample their objects from a deliberately broad range of scientific disciplines. A detailed study specifying one discipline can identify some important fine-grained processes that are excluded from such a coarse approach. Also, the authors' analysis makes no demarcation between different formats of scientific images. Moreover, measuring the surface area can obviously neglect the substance. Sizes of images in scientific journals are varied for many reasons. This is different from many other media (such as newspaper and magazines).

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<sup>86</sup> Lynch's study of visual representation in biology is a landmark exception, focusing exclusively on diagrams, see Section 2.6 of this thesis.

<sup>87</sup> Gross, Harmon, and Reidy, 2002.

<sup>88</sup> In all the articles sampled by the authors, the percentage of “numbered figures with titles” in the article has increased from 33% (period: 1901-1925) to 100% (period: 1976-1995). See Gross et al., 2002, Table 8.6, 173.

### 5.1.2 Quantifying the trends

This section interprets the results from the quantification of coverage of diagrams. Instead of employing the aforementioned approach that considers the surface area as reflecting the importance of diagrams, my quantitative approach examines proportion and frequency. As described in Chapter Three, *proportion* is defined as the share of a diagram type within the whole population of diagrams in each journal and in a specific period, and *frequency* is defined as the ratio of the number of diagrams to the number of visual items in a paper.

Figure 5.1 shows the frequencies (hereafter D/VI) in eight journals<sup>89</sup>. The 1990s and the 2000s are selected because these are the periods that have sufficient quantities of apoptosis papers for examining the changing patterns. D/VIs between the 1990s and the 2000s vary with the features of the journals, and some of the journals have relatively higher D/VIs. The most significantly high D/VI is seen in *Nature Reviews Molecular Cell Biology* (founded in 2000). This high ratio, I suggest, comes from its “review” function. In cell biology (as well as many other biological sciences), this function tends to rely greatly on visual means of communication.

Review papers in biosciences have special conventions of formatting (compared with original research papers). The generic purpose is to synthesise heterogeneous information produced by diverse practices so that the arguments can travel across different local research cultures. Diagrammatic representations are advantageous in conveying the integration of the heterogeneous knowledge<sup>90</sup>. Visual communication in biological reviews has been increasingly focusing on synthesising information, as the conversations within the expert community increasingly concern interaction and integration:

We are witnessing a powerful syncretic movement that has already generated a common conceptual and methodological ground for many basic biological sciences, which until recently were separated into distinct disciplines on the basis of approaches used or domains covered. (Palade, 1985, 1)

This quote is from the *Preface* to the first issue of the *Annual Review of Cell Biology* (1985), which identifies a need to “cover the merging fields” and disciplines that are “inextricably dependent on one another” (1985, 2). Such a “syncretic movement” embodies the notion of interaction between different systems of practice that Chang argues (2012, see Section 2.4 of this thesis) and nicely characterises the function of review papers. Mechanism diagrams are especially useful for synthesising heterogeneity and the most important diagrammatic representation in most of review articles. As introduced in Section 2.4 and reiterated throughout this thesis, mechanistic explanations for biological phenomena are meant to integrate multiple levels of entities and activities. The advantages of using diagrams for integrating information (see Section 2.4 and 2.5) are confirmed by the impressively high frequency of mechanism diagrams in *Nature Reviews Molecular Cell Biology* (Figure 4.2.5.4).

As new as *Nature Reviews Molecular Cell Biology*, *Nature Cell Biology* was founded in 1999 (data shown in Figure 5.1 has omitted 1999). While it is not a review journal and has a low-to-middle D/VI compared to the other journals, its relative frequency of mechanism diagrams is significantly high (Figure 4.2.4.5). The low-to-middle D/VI results from the omission of year 1999. When 1999 (the year of establishment) is included, the ratio appears high compared to the other journals (for example, see Figure 4.2.4.2).

Here I try to explain this difference with regard to the change of research scope, though no

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<sup>89</sup> See Section 3.2.1 for the detailed characterisation.

<sup>90</sup> See Section 2.5 for Bender and Marrinan's argument, which supports this view.

confirmed explanation is available at hand. This difference can be understood as either a contingency or a characteristic of a newly-established journal in a discipline that has been drastically expanding. Figure 4.2.4.3 clearly suggests that the mechanism type makes the most significant contribution to the difference of D/VI between period 1999–2005 and period 2000–2005. An explanation for such a difference is that, in the year of the journal's establishment, the authors tended to systematically picture the mechanisms of enquiry so that their discoveries could be (both virtually and visually) situated in the community of apoptosis research. In other words, a newly-launched journal in a rapidly-growing field might have preferred cell biologists *mapping* their discoveries onto the existing knowledge. This is comparable to Rasmussen's notion of knowledge mapping (Section 2.3), where novel findings are accepted by the research community through being mapped onto—and considered as commensurable with—the existing knowledge. In practice, cell biologists tend to design their next experiment according to their current location in the array of existing discoveries, and the array is normally visualised by synthetic diagrams. The visualisation of this array resembles a map in the sense that the discoveries are illustrated as the landscapes in the territory, where the territory is the virtual space of the mechanistic model. In such an image, the component entities and component activities are correlated with different kinds of sign functions<sup>91</sup>, making an integrative whole that represents the array of discoveries. The relationships amongst the components are the key features of the array of knowledge, and the relationships amongst the signs are the key features of the visual representation of the array. Section 5.5 and 5.6 shall further discuss this aspect.

While the D/VI varies by the scope of the journal, the importance of diagrams is told in all the journals surveyed from different aspects. Amongst the remaining six journals, there are (1) two journals exhibiting an obvious increase of diagram use from the 1990s to the 2000s, (2) two journals presenting a steady yet slightly increased D/VI, (3) one journal having a steady yet slightly-decreased D/VI, and (4) one journal having an obvious (but not statistically significant) decrease of diagram use. A growing tendency to employ diagrams (especially the mechanism type) can be extracted as the overall implication based on the following observations.

Firstly, the increased use of diagrams by the two journals suggests that diagrams increasingly take up the coverage in visual communication. Secondly, compared to these two journals, the three journals with steady D/VI have relatively established formats for the papers. Two of them have middle to high D/VI, which can suggest that the frequencies of diagrams have reached the saturation for the moment. One journal has low and steady D/VI because of its focus on local pathways rather than integrative mechanisms, which results from its concern of cancer therapeutics (Section 4.2.6). For the original research papers of this journal, the major part of visual communication must always prefer data images (eg. photographs and chart graphs) over diagrams. However, in this data-heavy journal, the coverage of diagrams is not really constrained by such a format, despite the rapid growth of data quantity during the past decades. Diagrams could have yielded the space to data images and been as low as seen in the early years (before 1990), yet the coverage of diagrams remains steady.

Only *The FASEB Journal* exhibits a notable decrease of D/VI from the 1990s to the 2000s. Section 4.2.8 has examined this decrease and maintained that this decrease is mainly due to the launch of a new article category, *FJ Express*. Similar to *Nature Cell Biology*, *FASEB*'s decrease in the overall use of diagrams is immediately related to its decreasing use of mechanism diagrams since 2000. While most of the journals surveyed increasingly employ the mechanism type in their visual communication, *FASEB* differs from the others by launching an article category that emphasises efficient delivery of novel findings (experimental results). Articles in this *Express* category do not

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<sup>91</sup> See Section 5.6 for the application of Wood's cartographic thesis (1992, 2010) to the analysis of mechanism diagrams.

even have page numbers when published online before printed<sup>92</sup>. While all types of diagrams are found in this category, Figure 4.2.8.8 shows that mechanism diagrams are reduced to the greatest extent compared to the other types. The decrease of diagrams in general is probably a result of changing the scope of the journal, and this change of scope from synthetic models to experimental data has most affected the mechanism type. This suggests that, in *FASEB*, the mechanism type is as important as in the other journals. In other words, while *FASEB* from 2000 does not exhibit a similar pattern of overall emphasis on diagrams, its reliance on mechanism diagrams is consistent with the general emphasis on visualising mechanisms as found in the other journals.

Although object and mechanism are the two prevalent types of diagrams in apoptosis research, the results also suggest that they exhibit relative changes of coverage through time. The implication is that when the researchers communicate with other specialists via visual means, they increasingly consider cell phenomena in the context of mechanism rather than object or morphology. Figure 5.2 shows the importance of both types in six of the surveyed journals<sup>93</sup>. Apart from the prevalent proportions of these two types, a more important message of Figure 5.2 is about the relative changes between them from the 1990s to the 2000s. It is clear that, in most journals, the mechanism type has more significant coverage than the object type. Meanwhile, it is noteworthy that even in *PNAS* and *Cell*, where the mechanism type does not have the largest proportions, the mechanism type still has grown in both proportion and frequency in parallel to the general decline of the object type.

The object type had its heyday in the 1990s. This is well-demonstrated by the quantitative results (see Figure 5.2 and 5.3. See Chapter Four for details of individual journal). In all the journals surveyed, the majority of object diagrams are always about schematic representations of macromolecules. Chapter Four has hypothesised that the popularity of object diagrams in the 1990s resulted from the blossom of technologies for producing data through manipulating genes and proteins. At the same time, novel visualisation technologies provided new visibility of genes and proteins. Three-dimensional visions of structures of macromolecules gradually take up the territory that used to be dominated by highly-simplified schemas and sequences made of letter abbreviations. Nevertheless, the communicative nature of these diagrams remained as “representation of objects”, despite their novel appearances. They are the representations of *static* things.

But biological phenomena are not static. They contain dynamic processes. Scientists investigate such dynamics of biological phenomena to develop explanatory models for it. Therefore, apart from object diagrams, visual communication in apoptosis research had to find a way to properly convey these non-static explanations. I consider the development of mechanism diagrams as the solution to the need of communicating explanations for dynamic phenomena. This development probably occurred in the late 1990s. Before the 1990s, mechanism diagrams in apoptosis field have been used to mainly visualise relatively simple causal occurrences (see the qualitative analyses of mechanism diagrams in Chapter Four). Yet they rapidly evolved since the 1990s to become vehicles capable of accommodating the complexity of explanatory models for apoptosis.

The relative changes of the two prevalent types suggest a shift of the focus of visual representation in biology from object to mechanism, from the morphology to mechanistic models, and from description to explanation. Figure 5.3 and 5.4 illustrate the growth of mechanism diagrams that quantitatively supports this argument in two ways. Firstly, the rising frequencies of mechanism diagrams parallel the declination of object diagrams. Secondly, wherever there is a rise in the

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<sup>92</sup> See Section 4.2.8. Normally, electronic versions of journal papers are published online prior to the print, and the page numberings are consistent between these two versions. But the *Express* papers only have doi numbers when first appearing online.

<sup>93</sup> Here, *Nature Reviews Molecular Cell Biology* and *Nature Cell Biology* are again excluded for not being suitable for long term comparison, yet the unsurpassed prominence of object and mechanism diagrams in these two journals can be found in Figure 4.2.4.3, 4.2.4.5, 4.2.5.3, and 4.2.5.4. It should be noted that, in these two journals, the mechanism type especially takes over the coverage of all diagrams.

frequency of the object type (*Journal of Cell Biology* and *Cell Death and Differentiation*), the mechanism type has a greater growth. That is, the mechanism type either increasingly takes up the previous coverage of the object type or prevails in expert communication faster than the object type does. The mechanism type not only is prevalent but also has a greater influence upon the overall patterns of diagram use.

## 5.2 Resemblance and beyond

The remaining sections of this chapter will qualitatively analyse the contents of the diagrams surveyed and develop the arguments on the special features of diagrams. This section argues that biological diagrams can function more than resembling entities. Section 5.2 and 5.3 shall discuss some general features shared between object and mechanism diagrams, though they obviously differ from each other in terms of their different focuses on static (object) and dynamic (mechanism) things. Section 5.4 will discuss the relationship between the style of diagrams and the state of technology. Section 5.5 and 5.6 will elaborate the features of mechanism diagrams: heterogeneous, synthetic, and powerful in engaging real-world practice.

For Lynch (1990), transforming things from photographs appears to be one of the most basic ways of making biological diagrams. This is observed not only in biological illustrations earlier than the mid-twentieth century but also in the fact that diagrams in the journals surveyed earlier than the 1990s tend to concern depicting the appearances of biological entities. However, as this section shall explore, achieving visual likeness is not always the purpose of producing biological diagrams. Even some of the object diagrams represent more than the appearances of biological entities. Furthermore, mechanism diagrams are produced to narrate and explain biological processes (which contain entities and activities) rather than simply portray the entities.

Figure 5.5A presents an example of such traditional kind of diagrams. Not much information is added to the drawings, while certain things are either removed or modified to produce a “transformative rendering” (ie. the diagram) of the kind described by Lynch (1988). The producer of this kind of diagram remakes the observations through highlighting important information and degrading irrelevant details on the one hand. On the other hand, a certain extent of visual similarity between the original sources and the diagrams is retained. The transformation process is to deliberately render a display of what the viewer should see. In this study, diagrams of this kind fall into the object type.

A somewhat evolved form of Lynch's transformative rendering is shown in Figure 5.5B. As mentioned in Chapter Four, this diagram is a decade later than Figure 5.5A and more advanced in terms of graphic technology. It exhibits a more structured and unified form. Although the real structure of intestinal epithelium (the object depicted here) indeed is composed of very tightly-arranged and highly-ordered cells, this diagram further “rationalises” such structure by using more uniform shapes that cannot exist in a biological environment. Also in this “rational” sense, the depicted cells are divided into shaded and white categories. An axis is added to describe the layered structure of intestinal villi. These added elements, such as the colouration and the descriptive axis, are intended to teach the viewer how to view this structure based on background knowledge. While the depictions have visual similarities to the real objects, they no longer focus on resemblance to reality. Such depictions produced with expert judgement (in Daston and Galison's language, see Section 2.1) are still faithful to reality in Lynch's sense (Section 2.6). As an example, Figure 5.5B shows how the highlighting of details works in transforming photographs to diagrams by representing the orderly arranged cells with uniform little shapes. This diagram also has a feature that Lynch might refer to as adding “measurements” to biological diagrams, namely, the addition of descriptive axis and words. In this study, I refer to such features as the addition of descriptive visual



tools that make the representations of objects structured and uniformed for analytical purpose, as the term “measurement” is inadequate for discussing a feature that does not necessarily involve quantification<sup>94</sup>.

But biological diagrams frequently go beyond visual resemblance to specific objects. Also, visual likeness can be as limited as seen in Figure 5.5C, yet remaining useful in correlating the message (the tissue structure in this diagram) with the target entities. As discussed in Section 4.2.2, this combination of photographs and diagrams on the one hand exemplifies “transformative rendering” and on the other picks up what Lynch leaves out in his study of biological diagrams. Namely, diagrams have more active functions in communication and are not necessarily one-way transformative renderings from photographs. In Figure 5.5C, the diagram adds information that is absent in the photographs (and by no means available in real-world observation). No visual technique is able to “transform” a histological photograph to such a diagram of structure without sourcing knowledge from other places than the photographs and the microscopic vision. The visual likeness is limited to the extent that the viewer's eye may have to go back and forth between the two histological photographs and the diagram. Nonetheless, the limited visual likeness is not the main reason for such an inter-referencing process. This is because resembling the entity is not the primary representational function of this diagram. Instead, the viewer has to simultaneously read the photographs and the diagram because the diagram tells something the photographs cannot provide (ie. tissue compositions artificially gathered and shown at once), and the photographs present something the diagram does not offer (ie. how a piece of stained epidermis really looks like under the microscope). This combination actively invites the viewer to learn ideas from *both* the photographs and the diagram. The viewer interprets the meanings of the whole by reading the dialogue between these two kinds of visual representation.

Similarly, Figure 5.6 also requires the viewer to inter-reference between the photographs and the diagram. It differs from Figure 5.5C in the sense that this diagram is really a transformation from the appearances of both the petri dish and the “divided zones” in the experimental design. Photographs are not the only sources of transformation. The dish diagram is a schematic drawing of the dish itself, where the dish photographs are the records taken during experimental process to show the growth of yeast. Inter-referencing is required to correlate the experimental design with the experimental results. Figure 5.5 and 5.6 share some features discussed so far—visual likeness between diagram and reality, inter-referencing between photograph and drawing, transformation and schematization in the process of diagram making—but these features are rearranged in each diagram according to the context of use. Thus no universal principle is available for making such seemingly “resembling” diagrams.

Visual resemblance is found to have diverse forms in this study. The majority of the object type can also be understood as a special kind of visual resemblance to the actual things, albeit in most of the cases the attempt to resemble is implicit enough to be taken for granted. This majority in the object type contains various forms of schematic representation of macromolecular structures, as seen in Figure 5.7 and 5.8. Chapter Four has shown that (1) representations of sequences of macromolecules (such as letter abbreviations and schematic pictures) are the most prevalent forms, and that (2) the other forms of representing macromolecules (such as ribbon diagrams of secondary protein structures and space-filling model protein diagrams) appear more frequently than other subtypes of object diagrams. It is problematic to say that these representations of macromolecules exhibit no visual likeness to the actual things, yet it is equally problematic to say that they are intended to merely resemble the macromolecular structures. In this study, they appear to be the intermediate products of mixing visual likeness and symbolic elements. I will return to this point below, in my discussion of the semiotic aspects of diagrams.

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94 My modification of Lynch's terminology has been explained in Section 2.6.

Taking Figure 5.7 as an example, the arrangement of letters in Figure 5.7A is intended to resemble the transmembrane structure of a protein, and the loops in Figure 5.7B are intended to resemble the “hairpin” structures of RNA. Such figurative arrangements render the “calligram-like”<sup>95</sup> appearances of the two diagrams. At the same time, some visual elements are used to signal that certain components are artificially named and classified by the scientists—the letters represent amino acids (in 5.7A) and bases (in 5.7B), the words describe cellular places (in 5.7A), and the short lines represent hydrogen bonds (in 5.7B). As a result, the main part of these two diagrams are filled with symbolic elements. These two diagrams only resemble the actual macromolecules two-dimensionally and very schematically, but such simplified resemblances have a function: showing the spatial relationships between the subunits of the molecules. This kind of diagram has gone beyond the relatively primitive focus upon visual likeness, yet it retains visual resemblance as a feature alongside the invention and addition of symbols. Figure 5.8 is another example of this kind. In the upper panel, the words and the graphs, such as the letter “S” (showing locations of beta-strands) and the small circles (showing positions of DNA-binding), are examples of symbolic elements representing artificial concepts and obviously have nothing to do with visual likeness. The arrow shapes (representing beta-strands) and cylinders (representing alpha-helices) are too schematic to be viewed as resemblances of the actual protein structures. These visual elements represent ideas constructed in the research process but not the resemblances to the entities.

Mechanism diagrams sometimes contain realistic depictions. But they frequently employ both symbols and visual resemblances, often to a much greater extent than the object type does. This is due to the synthetic feature of mechanism diagrams (see Section 5.5 and 5.6). Visual likeness is normally used by the mechanism type to contextualise the mechanistic models in biological environments. In many mechanism diagrams, even the most subtle visual likeness between actual entities and their depictions is sufficient for representing the context. This is plausibly due to the viewer's assumption (and thus the ability to interpret the representation) based on background knowledge. The composition of Figure 5.9A almost has nothing similar to a real cell. It lacks a boundary (cell membrane) and a cell-like shape (usually round and somewhat irregular), containing mostly words and arrows arranged in a structured manner. This diagram does not really resemble a cell, but the mitochondria icon turns it into a representation of the cell. The icon schematically depicts two key visual features of the mitochondria (double membrane and cristae) that are the essentially and critically iconic elements of mitochondria structure. As a result, the mitochondria icon gains its identity and functions even more than representing a cell organelle. Its location implies that the space under the horizontal long line is the inner environment of the cell and that the whole diagram represents a set of mechanisms occurring across the cell membrane. The mitochondria icon serves to “label” the space it is located in, i.e. the inner environment of a cell<sup>96</sup>.

Here I define my use of terms for different signs by using Figure 5.9A as an example. I follow the semiotic definitions for three different kinds of signs. In semiotic terms, icons are a particular kind of signs, which exhibit a similarity or analogy to the objects they represent. The American philosopher and semiotician Charles S. Peirce distinguished iconic signs from indices (signs that exhibit a physical contiguity with their objects) and symbols (signs that represent by convention)<sup>97</sup>.

95 Calligram is a kind of text art and might have originated much earlier than the twentieth century (Brown, 2013). Initially, the calligrams were poems written in graphic patterns. Such an artistic form of text is sometimes called “shape poem”, “pattern poetry” or “concrete poetry”. In biology, diagrams of genetic macromolecular sequences such as Figure 5.7 too have shaped patterns intentionally visualising something. However, the letters do not make any literary sense. They are discrete abbreviations (symbols) for molecules. This the main difference between calligrams and shaped diagrams of macromolecular sequences.

96 Section 5.3.4 shall further discuss this unique “labelling” role of mitochondria icons in anchoring the viewer's attention.

97 This thesis adopts Peirce's categories as heuristic tools to analyse diagrams, and is thus not concerned with a systematic analytical account of Peirce's categories in themselves. For a scholarly account of Peirce's semiotic categories and the evolution of Peirce's theory of signs, see Atkins (2013).

While this thesis tends to discuss icons, indices and symbols separately for convenience, it should be noted that they are not mutually exclusive to each other and can be found mixed in the visual components discussed. The results of this thesis also show that the continuity between different signs (as discussed in semiotics) is commonly seen in the visual elements of diagrams. Thus, the mitochondria representation is a predominantly iconic sign, as it shares some key visual features (double membrane and cristae) of the actual object it represents, but it also has an indexical role in 'pointing to' the cellular environment. Finally, as Section 5.3.4 will discuss, the choice of membrane and cristae as key features of the representation seems to gradually become a shared convention amongst biologists to convey the meaning of "cellular environment". Such mixed signifying functions are important for the meaning of the diagram as a whole. Moreover, indexical and symbolic components are essential in realising the representative function of iconic signs in specific contexts and in relation to specific representative goals. This is especially relevant to this study, where indexical elements (eg. arrows and letters for labelling) and symbolic elements (eg. chemical notations) are indeed functional to the overall iconic function of diagrammatic representations<sup>98</sup>. In Figure 5.9A, the symbolic phrase "plasma membrane" and the indexical, vertical line next to it together contribute to the iconic function of the horizontal line for representing the plasma membrane.

Mechanism diagrams before 1990 tend to depict the contexts of biological phenomena in a more resembling way compared with the cases later than 1990. Such depiction usually requires multiple iconic elements. Take Figure 5.9 as an example, where 5.9B (1989) is a decade and half earlier than 5.9A (2005). As explored in Chapter Four, early mechanism diagrams tend to resemble the actual appearances of biological objects. Some visual elements in Figure 5.9B are key to resembling a cell: the round shape, the double outline, and the slightly irregular shape in the middle. Similar to the mitochondria icon in Figure 5.9A, these elements remind one of the cellular environment. But they do not work the same way as the mitochondria icon in Figure 5.9A does. Instead, they act more explicitly and iconically in terms of resembling the cell. The closed and irregular round shape represents the cell more vividly than the straight horizontal line and the colouration in Figure 5.9A. Meanwhile, symbolic and indexical elements conveying abstract ideas can also be found in Figure 5.9B. Those ion exchangers are symbolised by black dots and words. The ion fluxes in different directions and on different membrane positions are symbolised by indexical arrows. Moreover, there are words, boxes and arrows inside the cell, describing a biological phenomenon, ie. the fall of intracellular pH. These symbolic and indexical elements work together with the resembling elements to render a new, explanatory meaning—explaining the regulatory system of intracellular pH. Such a synthesis of multiple elements results in the generation of new meanings.

The mechanism type is especially good at synthesising signs, whether the visual elements are visually mimicking the actual things (resembling, iconic) or not (symbolic and indexical). Apart from using symbols, mechanism diagrams tend to incorporate more indexical elements, eg. arrows, than the other diagram types. Such employment of the indexical function of arrows enhances the ability of mechanism diagrams to better encompass abstract ideas. Symbols conventionally represent abstract meanings, while arrows point to, and single out, the elements of the diagram that are connected by dynamic processes. Section 5.3.3 will discuss the versatility of arrow meanings. Section 5.5 and 5.6 will argue that the mechanism type especially possesses a synthetic ability of integrating visual elements that have different signifying functions: icons, symbols, and indices. Through such synthesis, mechanism diagrams not only portray the entities, just like the other diagram types do, but also *narrate* the processes that the entities are acting within.

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98 On the function of diagrams in this specific sense, see Ambrosio (2014).

## 5.3 Visual innovations

This section discusses four kinds of visual innovations extracted from the diagrams surveyed. Firstly, some visual elements are used as (quasi-)modules for constructing visual conventions. Such conventions (while used locally and temporarily) offer a visual consistency that helps the reader correlate the ideas conveyed by different diagrams. Secondly, biological diagrams import certain non-specialist elements and impose new meanings on them. These elements normally appear to be “fun”, but they can function more than decoration. This involves a process of shifting the meanings from non-specialist ones to professional ideas. Thirdly, arrows in biological diagrams are greatly versatile in terms of meanings. The plurality of their meanings suggests an inconsistency between the complexity of ideas and the development of new visual vocabulary. Finally, the mitochondria tend to be visually emphasised in a number of diagrams composed of basic elements and having simple styles. In many cases, such an emphasis does not convey scientific information and sometimes is even redundant. Such an odd emphasis has two possible explanations: (1) the special visual features of the mitochondria and (2) the centrality of the mitochondria in apoptosis mechanisms.

### 5.3.1 Modular use of visual elements

This section discusses a special way of using visual elements to create a consistency throughout the visual language of biological diagrams. This consistency is based on visual conventions that are formed locally and temporarily to black-box some concepts. Such visual consistency facilitates the reader's conceptualisation of ideas conveyed by the diagrams. The special way of using visual elements is the modular use of elements. This study borrows the notion of modularity from architectural design, using it to refer to the characteristic of having standardised units that can be combined and rearranged in various ways to construct different larger compositions<sup>99</sup>. Along with the sophistication of visual elements during the evolution of diagrams, some visual elements seem to be treated as (quasi-)modules and used repeatedly in various contexts. Some of the cases might not be true modules due to the lack of an obvious standard of constructing, yet some others seem to have relatively standardised core structures, being reused and modified with their core structures remaining unchanged.

The increasing accessibility to digital graphic technologies since the late twentieth century seems very likely to be an important factor of the emergence of modular elements in the diagrams. A guidebook to medical illustrations (Briscoe, 1990) in the early age of digital graphic techniques considers computer and printer as advantageous tools in scientific diagram-making, as both “many copies of equal quality” and “changes and additions” can be quickly and easily made. Also, “the size and relative dimensions of the computer drawing may be varied and it can be used in combination with other computer drawings” (1990, 166). Such features are advantageous because “a diagram which can be changed and extended is often valuable for communicating” (167). This guidebook, as written by a practitioner, does not explain why a diagram communicates well with the flexibility to be changed and extended. This section proposes that the enhancement of communicative function by modular use of the visuals is due to visual consistency. This consistency serves to establish a convention that aids the reader's conceptualisation of the contents.

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<sup>99</sup> For the definition of module in architecture, see Davies and Jokiniemi, 2008, 241; Porter, 2004, 123; Goode, 2009, 617. The notion of modularity is extensively applied to a range of disciplines in contemporary time. For example, see Porter, 2004, 123; Schilling, 2003. The exact meanings vary with different disciplinary uses. This study stays with the three basic ideas: (1) standardised units, (2) combination (and rearrangement) of the units to build larger compositions, and (3) various ways of combining and rearranging.

Modular elements usually are purposefully designed to represent particular meanings, yet some non-standardised cases can serve a similar modular function in other applicable contexts. The left diagram in Figure 5.10 shows less modular characteristics than the right diagram, as the shapes of its component elements that are rearranged to compose the new ones are not special enough to count as modules. For example, both the rectangles that construct integrin and the jagged lines that represent proteolysed collagen are basic graphs. Such shapes are used in a wide range of contexts, possessing nothing specifically designed to represent the entities. Nonetheless, the arrangement of these shapes serves as a quasi-module. The complexity of the arrangements becomes greater from the top picture to the bottom, where the modification of details and the addition of new elements are done on the basis of the top arrangement. This gradual rendering of more complex arrangements exhibits a visual consistency that signals the relationships between the four statuses represented.

The right diagram in Figure 5.10 contains modular icons specifically designed for particular meanings. Note that this whole set of diagrams includes three independent diagrams that are numbered as different figures in the original paper. The upper diagram shows the experimental design, and the lower two diagrams present two slightly different mechanisms. Although given the different contexts of use, it is obvious that these three diagrams share some central part in common. The core structure of a protein complex appears repeatedly, with (1) some of the component units being replaced by other kinds, (2) some of the units being rearranged, and (3) the whole complex structure sometimes being rotated. While the core structure seems not strictly standardised like most modules, such a repeated use and the rearrangement still exhibit simultaneously the stability of the core structure and the flexibility of reusing it.

In the upper diagram, the core serves to establish a local *convention* of the basic part of the protein complex. This convention is local because it functions temporarily within this paper. Throughout the original paper, the author repeats this core in different figures whenever the core structure is visualised, as if this icon is an established visual convention of representing the protein complex. This conventional icon fits into different functional contexts of diagrams (experimental design; mechanism), contributing to building the protein configuration in different ways. Therein the element serves as a module. Whether the author intends to do so or not, such a modular use of the visual element renders a *visual consistency* throughout the argument (paper).

To a greater extent, the visual consistency resulting from repeatedly using a drawing of hippocampus in Figure 5.11 exemplifies the notion of modular use. Two points should be noted here. Firstly, the left diagram is an object diagram, and the right one is an experimental design diagram. Secondly, these two diagrams are just samples taken from the original paper, which has more other diagrams employing the same “hippocampus module” in various sizes and different contexts. Similar to the icon of the core of protein complex in Figure 5.10, the left diagram (the object type) serves to establish a visual convention of hippocampus representation for temporary use throughout the paper. Diagrams serving other purposes follow this convention by incorporating this hippocampus icon, modifying it to different sizes and filling it with different colours. Throughout the paper, the hippocampus icons in many different sizes are nearly (if not truly) geometric similarities to one another. Given the publishing year (2003), digital graphic technologies certainly facilitate the transformation between these geometric similarities, eg. enlargement and reduction of the shapes. While the right diagram in Figure 5.10 (the one with the protein complex core) could also be drawn with computer, Figure 5.11 exhibits much sophisticated artistic manipulation. But the difference between these two diagrams does not result from their artistic skills or technology. Instead, their difference lies in their degrees of visual consistency. Figure 5.11 shows much attachment to the temporary visual convention (the hippocampus icon) in the way it repeats it, transforms it, and rearranges it. It has a stronger visual consistency due to this more obviously modular use of elements.

The above examples suggest that both the advances in digital graphic technologies and their wide

acceptance around the field of biosciences might have contributed to the emergence of modular visual elements. The new technologies make it easier to make visual conventions. Without the technologies, it would take much effort to produce serial diagrams containing multiple transformations of a visual module. Yet it is still worth maintaining that there is no confirmed causal link between the rise of novel technologies and the innovative way to use visual modules. The innovations in digital graphing seem to parallel the innovations of visual thinking, and such parallel developments are embodied in biological diagrams. As the technologies at hand increasingly facilitate diagram production, scientists increasingly find new ways to visualise biological entities that they once have conceived in other visual forms (for example, via first-hand intervention or textbook photographs). This process is simultaneously (1) the black-boxing of the concepts (into the newly constructed images) and (2) the mapping between existing and new visualisations. Then the newly constructed images become modules to be used in different contexts of display, serving as new visual means that others can use to conceive the entities. Thereby the visual modules become conventional. The hippocampus icon is a good example of scientists constructing an image for their object of enquiry and making it conventional—though the convention is temporary—across different contexts of visualisation.

### 5.3.2 Elements from non-specialist areas

This section discusses the communicative and epistemological roles of visual elements imported from non-specialist areas. A large number of visual elements in biomedical diagrams, such as simple geometric shapes, are imported from non-biomedical fields, but this study has a special definition for “non-specialist visual elements”. This term means visual elements that already have particular meanings, which are usually conventional, in contexts other than biomedical sciences. The meanings are not standardised but generally recognised by different communities, thus being free to travel across different contexts without change.

In the diagrams surveyed, typical kinds of non-specialist elements include (1) emotion icons (Figure 5.12) that represent emotional statuses, (2) scissors icons (Figure 5.13) that represent “cutting”, (3) death signs (Figure 5.14) such as skull, cross, and gravestone, and (4) analogous signs (Figure 5.15) such as seesaws and gears. These four kinds are popular in apoptosis diagrams. This should not be surprising, as one considers both the key role of apoptotic enzymatic activities (which “cut” cellular substances) and the metaphorical context of apoptosis notion itself (ie. cell suicide and natural fall of autumn leaves)<sup>100</sup>. These elements are not essential to professional communication, yet intriguingly, they are used every now and then. Are they intended to evoke sympathy of the viewer about the fates of the cell? Are they the evidence of biologists decorating specialist communication with a sense of humour? In this study, the explanation seems to include both.

On the one hand, such elements serve as a reflection of the “fun” side of visual communication in bioscience. Such a fun side implies the individuality and personality of the researchers behind the making of diagrams. On the other hand, this section draws two more important implications from the employment of non-specialist elements by biological diagrams. Firstly, the use of non-specialist elements in biological diagrams supports what Gooding argued (1990, see Section 2.2.3 of this thesis) that the establishment of new visual language in a professional field can happen through borrowing existing elements from other fields. In this study, both the cases of the “scissors” metaphor and the simple machinery (the fourth family) are good examples. Secondly, analogous signs in biological diagrams (eg. simple machinery) are sometimes inseparable with the analogy approach of visual reasoning process. For example, a seemingly “fun” image of seesaw (eg. Figure

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<sup>100</sup> As mentioned at the end of Section 4.2.6, the Greek name “apoptosis” was proposed by the researchers in a somehow metaphorical context.

5.15A) is likely correlated with the scientist's very conception of balancing two opposing forces in a biological system. Just like analogies are included in rhetorical tools for writing text, visual metaphors and analogies are two of the rhetorical tools deployed in visualisation. Just like analogies and metaphors in verbal form strengthen the rhetoric, visual analogies and metaphors make visual communication richer and more impressive. But this strength may be the least advantage of employing metaphors and analogies in the biological diagrams. As this section will argue, what really makes metaphors and analogies indispensable to biological visual communication includes (1) the mapping between existing and novel concepts and (2) the function of analogy in visual reasoning.

Some of the non-specialist visual elements are more about animating the component entities and activities. The sequential facial expressions in Figure 5.12B and 5.12C are from two different papers in different journals. They are from different laboratories in 1999 and 2003 respectively. Although given the different local contexts of production, it is likely that the later use of emoticons (such as Figure 5.12) is inspired by some precedents (such as Figure 5.12B). This is usually seen in the development of conventions in visual culture. It is also likely that the authors of these two diagrams have no direct link to each other, being unaware of the existence of each other's diagrams, but they both instinctively employ serial emotion icons. This might be because they have similar stories to narrate: the progressive changes of the cell from life to death. It is a visual convention to represent the healthy status with smiling faces and represent the decline with sad faces. The smiling face in Figure 5.12A is published earlier than both B and C, exhibiting an obviously hand-drawing style. Yet it functions the same way as the emotion icons in Figure 5.12B and 5.12C. None of these "faces" communicates essential information but aids the viewer's imagination of the narrative. Because emotion icons are universally used, the viewer realises at first glance that, in 5.12B and C, the storyline begins with healthy status and ends at the death and that the things surrounding the cell in 5.12A are good for cell health. Directive arrows in 5.12B and 5.12C also help the viewer understand the directionality and appear to duplicate the function of the emotion icons. However, if the arrows were removed, all the visual elements attached to them would lose their communicative function. The arrows actually compose the profound part of the diagrams by interweaving the words and the icons so that they together form the narrative of status change. On the contrary, the emotion icons do not have such a critical function but aid the storytelling in a different way, serving as the animation of cell's "personality". Such animation enlivens the entities drawn and makes them "characters" in the stories told.

Some non-specialist elements require a mapping between non-specialist meanings and specialist concepts. Such mapping is essential to developing new visual languages in specialist diagrams. Comparing the scissors icons in Figure 5.13 to the above emotion icons, the meaning of the scissors is more solid and specific. Icons like scissors travel regularly across the boundary between everyday and specialist contexts and gain new specialist meanings (eg. enzymatic cleavage). Here, the development of a new visual language (representation of enzymatic cleavage) requires borrowing an existing vocabulary (the scissors) from other fields. Such kind of development is not rare in the visual culture of science. Gooding discussed it (see Section 2.2.3) by using Faraday's example of imposing new meanings on visual elements borrowed from other disciplines.

While the everyday meaning of emotion icons is far different from their use in Figure 5.12, the everyday meaning of scissors icons is quite comparable to the activity of the enzymes. The informed reader, as having the background knowledge in the meaning of the icons (ie. enzymatic cleavage), may understand this representation in a mixed way. On the one hand, the viewer intuitively understands "cutting" from everyday experience. On the other hand, the viewer interprets the enzymatic cleavage in a biochemical sense. The viewer does not confuse the scissors icons printed on everyday goods with the scissors icons in biological diagrams, yet an important part of their understanding of the latter must come from the experience of encountering scissors signs in

everyday contexts.

Death signs (eg. Figure 5.14) more directly correlate the everyday meaning with biological representations, as these death signs represent the cessation of cell life. Both death signs and scissors icons increase in frequency since the spread of digital graphic techniques, though the use of scissors icons is considerably less than death signs in the diagrams surveyed. Technical barriers cannot explain this. Nor can the assumption that scientists attempt to reduce extravagant elements. If the scissors icons are considered as extravagant and better replaced with other visual elements, such as words and arrows, cell death could also be represented by simpler elements. However, death signs appear commonly in many mechanism diagrams whose enzymatic cleavage activities are *not* represented by scissors. For example, both the mechanisms in Figure 5.14A and 5.14B contain the cutting activities of caspases enzymes, yet both diagrams represent the cutting with arrows. Meanwhile, both diagrams use death signs to mark the destiny of the cell. Moreover, Figure 5.14B adds some text on the gravestone icon, vividly delineating the mechanism of apoptotic progress in a somewhat dramatic way. As the enzymatic cleavage and the cell death are equally crucial events in apoptotic mechanisms, the obvious prevalence of death signs over scissor icons requires further study to explain.

Analogies appear to have a notable place in the visual culture of biological diagrams. In this survey, they are commonly seen in the representations of mechanisms but not in the other diagram types. I argue that visual analogy in biological diagrams evokes the viewer's comparison between the concepts presented (usually embodied by tangible objects and machineries) and the meanings implied (usually abstract). Such a role is seen in both specialist and non-specialist visual communications<sup>101</sup>. The scissors icons in Figure 5.13 already exemplify this role of visual metaphors in mechanism diagrams, where the metaphorical icons act only as the component parts of the narratives. The two diagrams cited in Figure 5.15 present examples of visual analogies that embrace the whole mechanisms. Each part of the mechanisms, be it an entity or an activity, is positioned at a place that has an operational role within the wholes. The compositions of both diagrams are object-centred, depicting tangible and everyday objects (seesaw and gears) that operate as simple machines. These two kinds of machine are so familiar to the viewer in the most ordinary sense. Thus these compositions do not cause ambiguity. The strength of such diagrams is the clarity of the key messages. Unlike the reading process of many diagrams of biological mechanisms, the viewer of Figure 5.15 need not look for the starting point to follow the narratives. The viewer can quickly understand that Figure 5.15A is about “balance” and that Figure 5.15B is about “correlated and interdependent actions”. There are other details in these two diagrams to follow, but the technique of visual analogy transforms the key messages into coherent groups of ideas that can be efficiently grasped. The imposition of biological meanings on the existing and everyday visual elements again is comparable to Gooding's thesis on Faraday borrowing visual languages from other disciplines to convey novel concepts of physics (Section 2.2.3). In this sense, the establishment of the specialist meanings of these machines appears to be similar to the scissors icons. Firstly, scientists import an established visual element that already has particular meanings in other contexts. Secondly, the visual element is used in a new way that analogises the new meaning to the existing meanings. Along with the consolidation of the correspondence between new and existing meanings, the visual convention gradually shifts to the new meaning.

Yet the use of visual analogy in mechanism diagrams has another important implication that highlights the special role of *machine* analogy in visual reasoning about biological mechanisms. Visual analogy can play a more crucial role than a facilitative tool for effective communication. Analogy has long been considered to have a significant role in both demonstration and application of scientific theory<sup>102</sup>. It can be an irreplaceable part of visual reasoning: through mapping the

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101 For example of studies on visual communications in either area, see: Smith et al., 2004; Kadunz and Sträßer, 2004.

102 Hesse (1954) has elaborated the role of analogy in demonstrating both the self-consistency and the value of



components of an abstract idea onto the components of the visual analogy, the idea is turned into a seemingly tangible form and more easily understood. When biological mechanisms are concerned, this reasoning process can occur at some stages of conceptualisation. The term “model” widely used by mechanism-minded biologists for addressing their explanations is also suggestive. It is true that certain visual analogies are employed only after the conception of mechanistic ideas, but some other visual analogies are intertwined with one's reasoning process. In the case of Figure 5.15B, as the author mentions in the paper (see Section 4.2.7), the “gear” analogy certainly comes from applying an existing object to the purpose of conveying the interdependence between the activities. It is clear that the concept of interdependence appears prior to the use of the “gear” image. But in the case of Figure 5.15A, as well as countless biological diagrams depicting seesaws, it is hard to tell which comes first in the visual reasoning: is it the proposition of the balance between opposite activities or the image of a seesaw? Seesaw images embed a concept of “balancing”. Unlike the above cases that gradually shift non-specialist meanings to professional meanings, the mapping process between the machinery of seesaws and the notion of balancing opposing activities can be mutual. Using non-specialist elements thus means more than adding facilitative communicative tools. Especially in visual representations of biological mechanisms, the use of a machine analogy may imply the way that biological *mechanisms* are perceived and conceptualised by the authors. Such visual analogy is reflective—if not a part—of the reasoning process of decomposing and reassembling the mechanistic models for biological phenomena.

### 5.3.3 Plural meanings of arrows

This section argues that the differentiation of meanings and functions of arrows in biological diagrams is plausibly a response to the growth of complexity of scientific ideas but *not* the improving graphic tools. Amongst all the visual elements in biological diagrams, arrows are one of the most used ones. They also seem to have most differentiated forms and diverse functions. Such an extensive use of arrows is especially obvious in mechanism diagrams. So many different relationships amongst the components of mechanisms are represented by arrows that biological mechanism diagrams almost cannot function without arrows<sup>103</sup>. In a rapidly growing field like apoptosis, existing visual elements become increasingly inadequate to represent complex ideas. To overcome the ambiguity caused by the shortage of visual elements, several reactions may take place. For example, there are creative trials of rearranging existing icons.

Imposing plural meanings on the visual elements appears as another solution. This section will show the versatility of arrow meanings. In some cases, the researchers also capitalise on novel graphic technologies to develop new elements. They may even invent novel technologies to meet the need of visualising complex ideas. Also, sometimes there is a requirement for professional knowledge to decipher the arrow meanings. This is because the plurality and versatility of arrow meanings black-box some concepts due to the inconsistency between the growth of ideas and the development of arrow designs.

Here are some typical arrow meanings found in the mechanism diagrams surveyed. Mechanism diagrams normally synthesise various arrow functions, despite the arrow forms being similar or identical:

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prediction of scientific theories. In physics, analogy relates theory to the experimental results. However, she focuses on abstract analogy that cannot be pictured.

Previous studies of visual languages have also shown that visual analogy takes a significant part in human problem-solving process. For example, see Davies, Nersessian, and Goel, 2005.

<sup>103</sup> Although not explicitly presented in the quantification, the results of this study show that the mechanism diagrams sampled all contain arrows except for Figure 4.2.7.26.

- **Causal arrows** are the most seen functions of arrows that represent causalities between component activities.
- **Sequential arrows** guide the viewer's attention through biological processes. These sequential arrows are also used by the experimental design type to present instructional procedures.
- **Indicative arrows** link the entities depicted with their names. An example of indicative arrows is in Figure 5.16A, where the names of the ligands (eg. “TNF”) and the subunits (eg. “MORT1”, “TRADD”) of the two receptors are identified and associated with each other by the arrows. Indicative arrows are common in both object and experimental design diagrams.
- **Arrows showing movements** identify a change of location, such as translocation of proteins from the cytosol to cellular organelles.

A single diagram often contains different types of arrows. Figure 5.17A exemplifies this feature. The arrows ending with bars symbolise a “stop” effect of some molecules on some others. They are negative causal arrows that represent the “causing inhibition” effect of certain proteins. On the other hand, in the middle lower part of the diagram, there are positive causal arrows showing “effector caspase causing caspase substrate cleavage”. The vertical arrow linking the words “substrate cleave” and “cell death” is a sequential arrow, showing the order of cell events. In the right part, there are arrows showing the movement of protein Bax.

The above typology does not exhaust all the arrow functions in biological diagrams, as there are always arrows with meanings that are arbitrarily designated according to the messages of the diagrams. For example, in Figure 5.17A, the arched arrow linking “Bid” and “tBid” means that a structural change happens to the Bid protein and turns it into a truncated (ie. not full-length) Bid. Moreover, the two arrows linking “caspase substrate cleave” and “cell death”, as well as “DNA fragmentation” and “cell death”, actually mean more than the sequences of events. Because both cleavage of cell substances and DNA fragmentation are key signs of apoptosis in progress, these two arrows somehow imply the symbolic meanings of the two phenomena in cell death. They converge at the end of cell life.

The increase of arrow variety does not necessarily synchronise with the proliferation of arrow function. Many cases surveyed suggest that arrows in very similar or the same forms sometimes carry entirely different meanings. The aforementioned arrows in Figure 5.17A do not quite differ from each other in terms of appearance, despite their diverse functions (causal or sequential etc). The evolution of arrow forms seems to occur more slowly than the growth of diversity of arrow meanings. This is very plausible, for the growing diversity of arrow meanings is closely tied to the unregulated growth of the research field. While apoptosis research has grown exponentially during the past decades, the development of visual tools for conveying novel knowledge might have been behind. The advancement of graphic technologies might have facilitated the diversity of arrow form, but designing new elements to represent novel ideas is not merely a technological task. It is a human art. Novel technologies do not spontaneously invent useful visual tools to match the need of communicating novel knowledge, and it is a human job to fill in the gap between the complexity of meanings and the adequacy of representational tools. Section 5.4 shall further explore this topic.

Such gaps can make the interpretation of diagrams less intuitive. Figure 5.16B shows how imposing complicated and diverse meanings on similar (or the same) forms of elements can cause ambiguity and confusion. In Figure 5.16B, the uniformity of arrow form contrasts with the great heterogeneity of the information conveyed by the arrows. The diagram is about the mechanism of apoptosis progress through four stages. The arrows at each stage represent different activities, ranging from ligand-receptor binding to enzyme activation. But the arrows appearing at the same stages do not necessarily function likewise. What makes the visual language of this diagram even more

ambiguous is that, as the original caption of this diagram mentions, the arrows do not necessarily represent direct interactions (see Section 4.2.2). Also, there are some points where some of the arrows join each other being left blank without any symbol (for example, in the middle part, the arrow starting with “p53” and the arrow starting with “glucocorticoid receptor” join each other at the start of the arrow pointing to “CPP32”). All these features of this diagram show how confusing it can be to impose multiple meanings on a limited variety of elements. This diagram clearly names the key entities of the mechanism, but it is weak in conveying the relationship between these entities. Thus understanding this mechanism requires both background knowledge and the explanatory text. The viewer must ignore the uniformity of the arrow form and refer to other sources to differentiate the different arrow meanings, as if they were drawn differently.

To represent the increasingly complex perspectives for modelling biological phenomena, the forms of visual elements must evolve. Figure 5.16B is published in 1996, when discoveries about apoptotic mechanisms has begun to explode. Section 2.4 has reviewed that these discoveries originated from multiple research areas. The existing forms of arrows had to evolve to accommodate such a richness of perspectives. In this sense, the plurality of arrow meanings reflects the contrast between the limitation of existing representational resources and the growing complexity of ideas.

In some cases, it is the technology that evolves to overcome the shortage of visual elements. The limitation of conventional visual languages is explicitly pointed out by some scientists, especially those who take network and systematic approaches to modelling biological phenomena. Scientists who rely heavily upon visualisation of mechanisms are aware of the confusingly plural interpretations of visual elements. Some scientists in these fields have sought to solve this confusing plurality via improving computational techniques of graphic representation to standardise the visual languages<sup>104</sup>. Such efforts are nonetheless restricted to certain fields that employ computational modelling in diagram production. Given the current impossibility to standardise visual languages of biological diagrams, scientists (the viewer) usually compensate the ambiguity caused by the plurality of meanings of visual elements with background knowledge.

In the case of conveying dynamic activities but not static objects, the shortage of visual elements can be more challenging. This is suggested by comparing the two groups of arrows that respectively represent entities and activities in Figure 5.16A. This diagram is published in the same year with Figure 5.16B and also exhibits the versatility of arrow meanings. But the two different groups of arrow meanings in 5.16A are better differentiated from each other than 5.16B, as they have different sizes and positions. The group of arrows pointing *out* the subunits of receptors is visually distinguished from the group pointing *to* the directional process of apoptosis. The other point of this diagram is the different degrees of complexity between the representations of entities and activities. The processes are represented by relatively plain and simple elements (arrows) compared to the relatively complicated depiction of the two receptors. The development of new visual elements for representing objects seems to move faster than the development of narrating and explanatory elements.

In other words, the gap between novel ideas and new elements seems to be wider in the case of representing dynamic processes. This observation is common in the mechanism diagrams surveyed. It seems not difficult for the authors to create new representational elements for novel entities. In the case of composing visual narratives and explanations, the need for new representational elements rapidly grows along with the expansion of ideas. Such a need is harder to meet. Figure 5.16A contains two large arrows representing activities and imposed complicated concepts. The first one means a sequence of “activation of enzymes” and “enzymes cleaving death substrates”. The second one means “leading to apoptosis”. Contrary to such complexity of information imposed on

<sup>104</sup> For example of improving mathematical modelling to visualise mechanisms in standardised ways, see Kitano et al., 2005.

these two simple arrows, the small arrows surrounding the receptors mean the same thing: they serve to point out the structural parts.

The proliferation of arrow meanings may be treated as a sign of both the proliferation of knowledge and the growing complexity of mechanism research. The results of this thesis generally suggest that the arrow forms in mechanism diagrams become more diverse in recent years. In recent diagrams, different relationships and activities are increasingly represented by arrows in different colours, sizes, and shapes. This cannot be explained solely by the increased adoption of novel graphic technologies, since visual elements do not necessarily evolve until they have to. Normally, new forms of elements are developed on the basis of existing forms, and then the improved graphic technologies allow further developments. In sum, the evolution of arrow forms is a response to the growing richness of the ideas, and that this evolution is not merely an effect of novel technologies. Sometimes the relationship between the increase of novel ideas and the advancement of graphic technologies is reverse. This section has mentioned an innovative measure of introducing novel visualising software, which is an example of technology responding to the growing richness of ideas.

#### **5.3.4 Specially designed icons: the emphasised mitochondria**

Representations of the mitochondria appear to be emphasised in many of the mechanism diagrams surveyed. This emphasis is especially obvious in diagrams composed of simple visual elements such as words, arrows, and lines. Here, I clarify my occasional use of the plural noun (mitochondria) in a singular sense. Visual representations of the mitochondria normally are single icons that represent a *collection* of all the mitochondria in a cell but not any specific single mitochondrion. This feature of visual language seems to reflect the verbal language of biology. As explained in Section 4.2.6, in biological writing, the use of the plural term “mitochondria” is sometimes used to refer to all the mitochondria as a singular collection. Namely, the single icon is a representation for “the organelle” (which has a collection of singles), instead of a single mitochondrion. In this context, this thesis uses the plural term in the singular sense that refers to “the specific cell organelle” but not any single mitochondrion. This, incidentally, exemplifies the continuity between the iconic, indexical, and symbolic elements of this representation as I introduced in Section 5.2. The mitochondria representation is iconic because it exhibits, to a certain extent, a “likeness” with the objects it stands for. But in the context of the diagram its iconic function coexists with the conventional use that biologists attach to it when using it to refer to a collection of mitochondria in a cell.

This section discusses two possible explanations for the visual emphasis on the mitochondria (see Chapter Four for detailed examples). In many mechanism diagrams composed of simple elements, the mitochondria and the nucleus tend to be depicted in a more figurative way than the other components, and the depictions of mitochondria tend to be more figurative than the nucleus. The first explanation comes from the special visual features of mitochondria. Those features can be conveniently schematized and transformed to representational icons without causing ambiguity of the meaning. The second explanation is the centrality of mitochondria in apoptotic mechanisms. For example, the locating of Bax protein on the outer mitochondrial membrane and the permeabilisation of mitochondria are considered together as the point of no return in apoptotic progress. The subsequent release of cytochrome c is also one of the death hallmarks. This centrality of mitochondria may be reflected by the visual emphasis on the organelle in mechanism diagrams.

The visual features of mitochondria are special enough to inspire the design of icons. Its folded cristae and integral membraned structure not only make it very recognisable but also render possibilities of schematization. Comparing the mitochondria and other organelles (such as the Golgi

apparatus and the nucleus), it takes less effort to extract the visual characteristics from the structure of mitochondria. An oval shape can represent either the nucleus or other oval-shaped organelles, but a simplified drawing of mitochondria—an oval shape containing folded and irregular closed shapes inside—can only be a representation of mitochondria. That is, icons of mitochondria have a relatively stable meaning that does not change in different visual contexts, despite that their styles may vary.

The variety of styles of mitochondria icons sometimes suggests that a “black-boxing” process occurs in both the imposition of meanings and the development of visual conventions. Figure 5.17 presents three examples of mitochondria icon. Only one of them (5.17A) features a three-dimensional effect. Given the font style of some embedded words (“extrinsic” and “intrinsic”), the use of this effect may be more about complying with the overall style than emphasising the three-dimensionality of the organelle. Only one of them (5.17C) depicts the inner structure (the cristae) in a mimetic way, while the other two roughly represent the cristae with closed irregular shapes. Such highly-sketchy representations are quite common in mechanism diagrams, as seen in Figure 5.18 and many other diagrams cited in Chapter Four. Mimetic depictions (as seen in Figure 5.17C) appear less frequently. But interestingly, the meanings of these two different styles of representation appear equally straightforward. The trained viewer who is familiar with the visual conventions of biological diagrams can intuitively recognise the identical meanings of these two different icons. The closed irregular shapes might have derived from mimetic depictions, for visual resemblance is a tradition of making biomedical diagrams (Section 5.2 has discussed this tradition, and Section 2.6 reviews Lynch on the transformation required to produce the resemblance). Thus the trained judgement of the viewer seems to automatically erase the process of developing visual conventions, blurring the visual differences between these two styles of mitochondria icons. In this case, not only the imposition of the meaning but also the derivation of novel icons from existing ones are black-boxed.

While new styles emerge, traditional styles do not become obsolete. Diagrams later than 2000 still contain mitochondria icons that depict the structure in a resembling way. Good examples include Figure 4.2.1.18 (2001), Figure 4.2.3.14 (2003), and the mitochondria “template” used throughout *Nature Reviews Molecular Cell Biology* (established 2000). Mitochondria icons keep existing in various forms, while the variations always preserve two key characteristics: closed oval shape and folded inner structure. In fact, there is only one key structure (the cristae) that exclusively characterises the representations of mitochondria. Figure 5.17B exemplifies how this structure makes a mitochondria icon special: without the irregular shape inside, the ellipse representing the mitochondria cannot be distinguished from the other ellipses that represent proteins.

The cristae structure can be transformed differently with different technologies, art skills, and aesthetic considerations. Some of the transformations are sketchy to the extent that they do not have the feature of closed shape and become curvy lines (see Figure 4.2.2.17). Nevertheless, even this highly simplified representation somehow exhibits resemblance to the appearance of cristae—the curvy lines subtly resemble the folded cristae. Some rare cases go to the extreme, such as Figure 5.18A. This mitochondria icon entirely abandons depicting “foldings”, not even in the sketchiest way. This icon is more like a representation of the nucleus than the mitochondria. But such extremes are rare amongst the diagrams surveyed and have a different implication. Namely, the mitochondria as a cell organelle is central in the apoptosis mechanisms and more likely to be emphasised than the nucleus. Thus this visual language has no ambiguity. Before discussing this implication below, I sum up the first explanation for the visual emphasis on the mitochondria. Their special and notable structures (mainly the cristae) are convenient for the scientists to schematise and transform. The meaning of visual language is stable across different depicting styles. The viewer understands the visual language based on professional judgement, which opens the black-boxed process of developing visual conventions.

The second explanation for the visual emphasis on mitochondria refers to the importance of the

mitochondria in apoptotic mechanisms. Examples from this survey show that, while many mechanism diagrams composed of simple elements did not have to depict the mitochondria in an exclusively figurative way, they do so. Replacing most of such mitochondria representations with either words or basic shapes does not alter the messages of the diagrams, and the mitochondria tend to be the most extravagant (yet not always functional) visual elements. In Figure 5.18B, the damage to the mitochondria (represented by the word *damage*) caused by translocation of Bax protein is not visually obvious enough at a glance, as this icon can also represent the normal state of mitochondria. This diagram does not provide a visual contrast between the normal and the damaged states, which, for example, is vividly “cartooned” in Figure 4.2.4.9A. The resembling depiction in Figure 5.18B does not necessarily convey the key message, yet the mitochondria are the most figurative element in the diagram.

Similarly, the mitochondria icon in Figure 5.18A does not necessarily have a role in communicating important messages. Meanwhile, it has a somewhat misleading appearance that is very similar to the visual convention of another large and double-membraned organelle, ie. the nucleus. Although the viewer can recognise its meaning by tracking its location in the pathways, the descriptive label “mitochondria” underneath it appears to be more helpful to the viewer's understanding of this meaning. The most important function of this mitochondria icon is to convey the large size and double-membraned structure of the organelle, but this basic information is irrelevant to the key message (and obviously known by the trained viewer). By contrast, Figure 5.18C may have a stronger reason to visually emphasise the mitochondria with an iconic drawing. Given this drawing, the influx of calcium into the matrix (the inner part of mitochondria) and the release of cytochrome c from the intermembrane space are visualised so clearly that no description word is needed. This part of diagram exemplifies the communicative function of visualisation that is (1) “worth a thousand words” and (2) independent from words. The difference in communicative function between these two mitochondria icons in Figure 5.18A and 5.18C implies that the mitochondria are emphasised not because the authors want to exclusively make resemblances to them, but because the mitochondria are central to particular mechanisms.

In conclusion, figurative and extravagant mitochondria icons are visually attractive in diagrams that have simple styles. Perhaps this visual attractiveness serves to stress the centrality of the mitochondria in apoptosis mechanisms. On the other hand, if the author wants to employ slightly sophisticated elements in an apoptosis diagram composed of simple elements, and if the concerned pathways involve the mitochondria, the mitochondria are very likely to be visually emphasised. This is because they can be drawn in highly simplified forms yet retaining their key characteristics. Indeed, the mitochondria icons per se may be more decorative than communicative elements (see Figure 5.18A for the overlapping functions between the icon and the word), appearing replaceable by simpler elements, such as words and basic shapes. To find out whether or not the mitochondria are as emphasised in other biological fields as in the apoptosis field, further comparative study is needed. If this is the case only in apoptosis research, it can be assumed that such extensive design of mitochondria icons in apoptosis diagrams implies a scientific purpose to highlight the critical role of this specific organelle.

## 5.4 Technology is not everything

This section argues for two points on the relationships between novel technologies and the evolution of diagrams.

Firstly, the emergence of advanced graphic technologies around the 1990s had a greater impact on the object type than the other diagram types. However, while the advanced tools have indeed brought novel styles to the visualisation of biological objects (especially those “invisible”

macromolecules), the aspects of visualising the objects are not necessarily changed by novel technologies. In fact, most of the aspects of visualising macromolecules have existed before the emergence and spread of digital tools. Thus the real impact of novel technologies on the visibility of biological object diagrams is more about increasing the use of sophisticated forms of visualisation.

Secondly, the configurations of mechanism diagrams are not changed by new graphic tools, even though the visual elements may be drastically changed. Using verbal language as an analogy, the visual languages of biological diagrams are influenced by new graphic technologies in terms of rhetorical elements but not the *grammar*.

In sum, this section argues that technological innovations in visualisation do not necessarily lead to visual innovations. Novel tools do bring novel elements, but these elements are not necessarily used in an innovative way.

#### 5.4.1 New tools and the object type

The most notable effect of advanced graphic technologies on biological visualisation is about the increased coverage of novel representations of objects, especially at macromolecular and cellular levels. Most of the other diagram types either confine the advanced visual tools in decorative function or do not even use them at all<sup>105</sup>. Figure 5.19 provides typical examples of novel representations of macromolecules produced by computer software. These representations of proteins are novel because, at least in this survey, such diagrams had not been widely produced until the 1990s. By the late 1990s, such representations have become a basic part of structural information that is normally provided in papers targeting specific proteins (ie. the titles contain the names of specific proteins, and the papers investigate the roles of the proteins in apoptotic pathways).

The examples in Figure 5.19 represent proteins from different aspects. The upper left diagram shows the three-dimensional structure of a dimer protein called “14-3-3”, and the original caption calls this diagram a cartoon. The upper right diagram shows the ribbon-like appearances of the protein “sheets”. The lower diagram shows a ribbon diagram and a surface representation of the protein, where a surface representation means a three-dimensional visualisation of the surface topography of macromolecules. The use of colours varies by the scientists' choice, and most of computer software for macromolecule visualisation can do the colouration for both differentiating and emphasising purposes. The access to the software is increasingly common, as the resources of macromolecule database are increasingly available online. Scientists can visualise the structures and export diagrams according to the desired aspects after obtaining the data of structure determination. When the representations of macromolecular structures constitute a major part of the object diagrams since the 1990s (see Chapter Four), such novel representations not only enrich but also seemingly transform the visibility of the object type.

Nevertheless, are they *really novel* representations? Taking the protein structures as an example, most (if not all) of these aspects have been invented before the emergence of computer graphic software. Nowadays biological papers tend to contain nicely-coloured three-dimensional diagrams of ball-and-stick models, ribbons, space-filling models etc. The easy access to novel technologies makes these representations a typical part of visualisation in specialist communications, but the underlying concepts, in fact, have not gone much farther than half a century ago. Ribbon diagrams serve as a reflective example of the contrast between the advancement in technologies and the

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<sup>105</sup> For example, in many experimental design diagrams cited in Chapter Four, experimental animals and instruments are illustrated in traditional ways that exhibit not much difference from hand-drawn illustrations in pre-computer era.

stability of the aspects of visualising objects. In the late 1960s, there have been efforts to create a new aspect of illustrating protein structures. The “ribbon” appearances of a full range of secondary protein structures have first appeared by the end of 1970s and published in 1981 (Richardson, 2000). The creator of full-structure ribbon illustration, scientist Jane Richardson, describes her resorting to ribbon-drawing in a review paper: “I needed a better way of illustrating the three dimensional structures in order to show the comparisons and classifications directly.” (Richardson, 2000, 624) Then she went through a long and committed process of learning and practising illustration. This process of inventing new ways of visualising proteins, therefore, was driven by scientific needs but not design technologies. Of course, all the successful trials, including Richardson's and her precedents', are all hand-drawn. It is very interesting that, near the end of her review paper, Richardson points out:

As computer graphics became more powerful, effective programs were gradually developed to produce ribbon drawings *quite similar to my hand-drawn ones*. (2000, 625)

I highlight the key phrase in italics, for it intriguingly implies that the direction of technological innovation is toward what has been developed by hand. This does not mean that technological innovations are moving backwards. Instead, the implication is that the progress in visual technologies in this area is about visualising useful traditions in more convenient and accessible ways. As presented in Figure 5.20, those early hand-drawn ribbons do not differ from the computer-drawn ribbons in Figure 5.19 in terms of their design concepts. They might look slightly different in colouration and style, but the computer-drawn ribbons are just the machine-produced version of the hand-drawn ones. Richardson herself has also switched to computer software for generating ribbon diagrams. It is obvious that nowadays scientists need not immerse themselves in the painstaking practice of hand drawing in order to visualise their proteins. It is also obvious that, since the spread of digital tools, scientists increasingly include ribbon diagrams in their publications, making the “ribbon vision” for proteins a normal element of biological visualisation. If the space of image is limited, scientists probably prefer sophisticated ribbons over basic forms (such as sequences). As shown by the results in Chapter Four, in review-oriented journals such as *Nature Review Molecular Cell Biology*, there is not much room for visualising amino acid sequences (usually in form of letter abbreviations), where ribbon diagrams and other software-generated representations of structures are the majority.

Richardson considers the two most crucial advantages of computer drawing as (1) being “enormously easier” and (2) having the capability to allow “interactive rotation of the molecules” (625). Based on her opinion, I argue that it is both the user-friendliness and the interactive feature that make ribbon-drawing programmes *novel*. The ribbons per se do not *look* different through decades, while the increased possibility to produce larger quantities of ribbons with greater accuracy has profoundly made the visuality of object diagrams much richer than the time of invention of ribbon representations.

Similar stories have occurred in other cases of protein structure diagrams. Section 4.2.2 has presented a “helical wheel” diagram (Figure 4.2.2.6A) produced with new technology in the 2000s. The invention of this way of representing protein structure, however, dated back to the 1960s (Schiffer and Edmundson, 1967). Just like the ribbon story, both the concept and style of representing protein structures with wheel diagrams remain the same through decades, despite that the tool has been shifted from manual to digital and become widely accessible on the internet. In addition to ribbon and wheel diagrams, some other structure diagrams also have early origins: space-filling models (Figure 5.21A), ball-and-stick models (Figure 5.21B), and three-dimensional drawings of chains (Figure 5.22). These models were even developed earlier than ribbon diagrams. All the diagrams in Figure 5.21 and 5.22 were published between the early 1960s and the early 1970s. Figure 5.22 are similar to Figure 5.19A in terms of the three-dimensional styles of chains, and the surface representation in Figure 5.19 (the lower right image) shows influences received



from both ball-and-stick (Figure 5.21B) and space-filling (Figure 5.21A) models. The early models have long been educational tools that aid the learning of spatial arrangements within proteins. More importantly, they have been used to communicate protein structures to the public, given that Figure 5.21 and 5.22 are cited from a popular science magazine *Scientific American*. In other words, these representations of protein structures are long-established visual conventions that have gone beyond specialist communication. They are not anything new in the era of digital visual culture. Yet not until recently have three-dimensional and colourful drawings of these models massively appeared in biological papers (and perhaps in other communications not covered by this study).

Concluding from the history of ribbon diagrams, advanced technologies change the visuality of object diagrams not merely because they create new looks of the objects but mainly due to their capability of conveniently drawing visual traditions that used to be too sophisticated to produce widely around the world. On the other hand, the basic forms of representing macromolecules are not influenced by novel tools in terms of aesthetics. The simple style of representing sequences, such as Figure 5.21C, is still frequently in use. As seen in Chapter Four, such simple style of macromolecular sequences is one of the most common sub-types of object diagrams. Such linear representations still appear more frequently than three-dimensional representations because of their function to convey basic yet important information. However, they are somehow giving way to three-dimensional representations.

Thus the real impact of advanced tools is about the increase of sophisticated representations of macromolecules. This impact refers to not only the increased number of representations but also the increased frequencies of employing such representations for various purposes. Such representations become a new kind of visual elements, serving different functions in different contexts of use. Figure 5.23 provides two different examples of using computer-generated images of macromolecular structures in two different contexts: mechanism diagram (Figure 5.23A) and object diagram (Figure 5.23B). Figure 5.23A uses the ribbon images to contextualise a discovery. Figure 5.23B embeds two representations of macromolecules in a higher-level structure to not only contextualise them but also make a visual and direct comparison between them. Both examples use basic visual elements to picture the other parts and visually emphasises the molecular structures.

Figure 5.23A represents a mechanism containing two forms of a protein Grx2: the left “holo” form is inactive, and the right “apo” form is activated to be catalytic and anti-apoptotic. The original paper does not show interest in structure simulation of this Grx2 protein. Nor does it mention the full sequence apart from the catalytic site of the protein. The important discovery of the paper is about the bridging part (the iron-sulfur cluster,  $[2\text{Fe-2S}]^{2+}$ ) located centrally in the holo form. Thus the core chemical structure belongs to the key message, and the ribbons represent the background knowledge. On the right side, the three reactions and consequences correlated to the right “apo” form are illustrated in a quite schematic way. This illustration is barely related to the details of the ribbons. In sum, the two forms of Grx2 could have been represented with schematic drawings (or basic geometric shapes) rather than ribbons. But there are at least two possible reasons for using the ribbons. Firstly, the identification of the central iron-sulfur cluster and its role is an important discovery of the paper. Embedding the chemical structure of this cluster in the ribbon is to contextualise this discovery. The second reason may be simply adding decoration, where novel visual tools conveniently offer decorative elements that have both scientific and aesthetic values.

Figure 5.23B is an object diagram comparing two kinds of transmembrane ion channels. The key message is the structural similarity between the two channels. Namely, the two channels have similar pore linings (where ions are permitted to flow through). The original paper describes this similarity as that the left channel (MscS) is a “striking resemblance” (2004, 5590) to the right channel (VacA). Such resemblance allows the author to test the application of a modelling algorithm with MscS, where the algorithm is to be used for VacA modelling. The resemblance is a

significant finding not just because of the obvious likeness between the two channels. Also, the author has not assumed any structural similarity due to the very difference between their amino acid sequences. Here, a diagram of structural comparison has an important communicative function: it shows simultaneously the different sequences and the similar pore lining structures. Through arranging the two depictions of channels next to each other against the same background (the double membranes), both the difference and the similarity are conveyed without much need for verbal description. They simply *look* similar. This is the key discovery. The other point of this parallel display is about the exactly opposite orientations of the helices in these two channels. The helices of MscS channel have their C-termini in the cytoplasm, and VacA helices have their N-termini in the cytoplasm. All such information is conveyed and emphasised in the simple composition, where the representations of the membranes are reduced to merely two lines, and the different spaces are symbolised just by words.

These two examples in Figure 5.23 again suggest that advanced technologies change biological visualisation through enhancing the convenience of using sophisticated representations of objects as novel visual elements. The representations themselves do not have novel looks, but they are now more easily produced than the age when they were invented. As suggested by the ribbon diagram story, the inventions of hand-drawing and computer techniques for ribbon diagrams are both driven by scientific needs. One may argue that advanced technologies affect the way scientific ideas are visualised, yet one must be careful about suspecting any cause-and-effect relationship between novel art tools and the change of scientific visualisation. Co-evolution of art and scientific tools is not new in the history of scientific visualisation (see Section 2.2 for the example from geological sciences). The developments in art and science have long been intertwined in scientific communication. Novel technologies do not change such an intertwining relationship. Instead, they reinforce this relationship with the enhanced convenience of using visualisation as a component of research method.

#### 5.4.2 New tools and the mechanism type

This section discusses another point on the relationship between novel technologies and the evolution of diagrams. The case is the mechanism type, which is very different from the object type.

This case suggests that the grammar for visual language does not change with artistic tools but scientific ideas. This is probably due to the fact that mechanism diagrams are made of complex components: representations of entities, activities, and their multi-level relationships. While the entities can be represented by novel elements created by advanced technologies, the activities and the relationships are mainly represented by the compositions. The compositions serve as the syntaxes for the visual language, which represents the configurations of the mechanistic models. A number of mechanism diagrams surveyed support the argument that advanced technologies do not have profound impact on the mechanism diagrams, except for the creation of new (and mostly extravagant) elements. The examples have two features. Firstly, basic and sophisticated visual elements coexist within the same images. Secondly and importantly, even if the diagrams employ visual elements generated by new technologies, their compositions follow certain traditional narrating rules and do not necessarily arrange the novel elements in novel ways.

The four mechanism diagrams in Figure 5.24 and 5.25 demonstrate the gap between advancement in graphic tools and the relatively stable convention of compositions. I outline some parts of the diagrams with grey dotted lines to show their overlapping components. Comparing these overlapping parts, it seems that these four diagrams share certain conventional ways of arranging the visual elements, whether or not the elements are aesthetically different because of the

employment of new technologies. That is, the advancement in graphic tools does not necessarily change the visual grammar for narrating the mechanisms. The four outlined pathways are very similar—and even identical at some point—in terms of both the entities and the activities. They all involve the following: (1) translocation of Bax protein from the cytosol to mitochondria, (2) increased permeability of the mitochondria and release of cytochrome c to the cytosol, (3) formation of apoptosome and subsequent activation of caspase-9 by the apoptosome, (4) activation of caspase-3 by caspase-9 and subsequent cleavage of cell substrates. Here, the formation of apoptosome is not depicted in all these diagrams and needs a bit explanation: apoptosome is composed of cytochrome c, Apaf-1 protein, and the inactivated pro-caspase-9. This formation cleaves pro-caspase-9 and turns it into the activated form (caspase-9). Therefore, although Figure 5.25A does not explicitly provide information about the apoptosome formation, which is explicit in the other three diagrams, the activation of caspase-9 (represented by an arrow pointing from cytochrome c to caspase-9) clearly includes the prerequisite formation of apoptosome. All these diagrams are published in the era of emergent graphic technologies (Figure 5.24A: 2005; 5.24B: 2000; 5.25A: 2003; 5.25B: 2005), yet they all narrate the pathways with conventional arrangements, without adding extra aspects. Meanwhile, apart from the obviously extravagant drawings in Figure 5.24A, the other three diagrams employ very basic elements: words, arrows, lines, and circles<sup>106</sup>.

The impact of new graphic technologies is embodied by the extravagant elements in Figure 5.24A (eg. the inner space of the mitochondria, the release of cytochrome c, and the structure of apoptosome and its component proteins), which do not really convey technical information. These elements are seemingly sophisticated representations of objects like the ribbons in Figure 5.23B, but they do not have a communicative function comparable to Figure 5.23B. What really conveys the message is still the conventional composition or the grammar. Unlike Figure 5.23B, the techniques used to generate the icons in Figure 5.24A are not part of the scientific process. The ribbon representations in Figure 5.23B are not extravagant but essential. The icons in Figure 5.24A are the contrary case. Although their appearances are inspired by scientific discoveries, they are just decorated representations of the objects. New graphic tools do not change the composition of mechanism diagrams but only facilitate aesthetic manipulation. The overlapping parts between this diagram and the other three imply that these extravagant icons are *replaceable* by basic elements.

Figure 5.26 again demonstrates that, while advanced graphic technologies add vividness to certain visual elements and facilitate the design of new elements, mechanism diagrams are mostly composed with traditional visual grammar. The visual grammar is not easily altered much (if any) by new technologies. Some parts of Figure 5.26 are obviously products of advanced graphic tools, eg. the three-dimensional effect of the icons for HSC (hepatic stellate cells) in the lower part of the diagram, the size modification of these cell icons, the gradient coloration of the arrows, and the pattern coloration of the icons for KC (Kuppfer cells). In addition, the icons of cell nuclei of normal Kuppfer cells (left image) are round and large, where some of them turn into small particles (right image) and serve to represent fragmentation and condensation of cell nuclei during the change from normal status to apoptosis. While given all these computer graphic features, the main message of this diagram is conveyed in a traditional manner. The key information is about the role of a reagent SC-236, and this information is represented by simple elements (such as the arrows and the words in the right image). The arrangement of the arrows and the words is also simply traditional. The colourful elements produced with advanced tools, such as the icons of HSC and KC, are arranged in a traditional composition, too. This diagram contains a clear contrast between the computer-influenced design of elements and the traditional composition. These two features coexist within the same diagram, but the narrative of the mechanism is mainly conveyed by the traditional feature. Again using the analogy to verbal language, the rhetorical elements of the visual language of

<sup>106</sup> The mitochondria icons stand out amongst these basic elements in Figure 5.24B and Figure 5.25. Such visual anchoring effect of mitochondria icons has been discussed in Section 5.3.4.

mechanism diagrams are newly developed by novel tools, but the *syntax* does not go beyond what has been established before the emergence of digital technologies.

## 5.5 Mechanism diagrams: synthesising heterogeneity

This section argues that mechanism diagrams synthesise heterogeneity. Amongst all types of diagrams analysed in this study, the mechanism type especially exhibits a synthetic quality. This study considers that such synthetic nature of mechanism diagrams results from the intermediate involvement of diagrams in the practice. Biologists working in contemporary culture of integrating multi-perspectives are trained to interpret visual synthesis of heterogeneity. In Chapter Two, I have introduced the notions of synthesis and heterogeneity (Section 2.5), as well as the notion of integrating different systems of biological practice that does not reduce any of the component perspectives (Section 2.4).

The heterogeneity has multiple layers. This section discusses four of them: information, sign functions, data-diagram uniting and inter-referencing, and supra-perspectives.

### 5.5.1 Heterogeneous information

This section discusses the first layer, ie. the heterogeneity of information. Meanwhile, due to this heterogeneity of information, the component visual elements are also heterogeneous in terms of both style and sign function. Section 5.5.2 will discuss this layer of heterogeneity coming from the visual elements.

Biological mechanisms (as explanatory models for specific biological phenomena) have an integrative feature. This is because of the inter-field and inter-level features in the practice of developing mechanism models. Previous studies on biological mechanisms have pointed out these features of the practice through categorising both the information and the types of integration (Craver and Darden, 2013. see Section 2.4). There can be information of space, time, entities, and activities. All of them are to be integrated. The integration can occur at the same scale of space and time, or across different spatial and temporal scales. Importantly, the integrated information components are heterogeneous because they are retrieved from different fields. It is obvious that no single project in one field is able to completely host the mechanistic explanations for the subject matter. Several historical and philosophical studies on biological mechanisms, such as Bechtel (2006), Bechtel and Abrahamsen (2007), and Craver and Darden (2013), have discussed the “interfield” nature of the development of mechanistic models in biological sciences. Bechtel and Abrahamsen focus more on the encounter and integration between cell biology and biochemistry. Craver and Darden explicitly maintain the multiplicity and heterogeneity of information in biological mechanisms, when they discuss the interfield nature of mechanism study:

The science of biology must be integrated because it deals with a domain of heterogeneous phenomena, because mechanisms span multiple levels, and because mechanisms often operate at the across different time scales. (Craver and Darden 2013, 182)

That is, when biologists develop mechanistic explanations for specific phenomena, they must engage different explanatory projects from multiple fields. Due to the multi-level features of the subject matters (the phenomena to be explained), different explanatory projects must involve different (1) spatial scales, such as molecular and tissue levels; (2) times, such as events occurring at different stages of a process; and (3) time scales, where a completion of biological events can span from minutes to days. Through interweaving all this information, scientists build integrative

explanations that not only involve multiple levels (of space, time, activity, and entity) but also “form bridges” (2013, 182) between the fields involved.

Inter-field synthesis in the practice of biological mechanism research is straightforwardly reflected in Figure 5.27. Because inter-field practices are integrated in the development of this explanatory model, the perspectives are retrieved from different fields of interest. Each perspective contributes to the model with different information. This diagram contains two sets of visual elements, one represents biochemical reactions (the chemical formulae), and the other represents cell biological events (the words and arrows on the top, eg. “DNA damage”). Thus the model spans two spheres of knowledge: biochemistry and cell biology. Via pulling out the arrows directly from the biochemistry sphere to indicate the processes of cell events, this diagram smoothly correlates the biochemistry sphere with the cell biology sphere, making them both the components of a cohesive model.

Figure 5.28 is in a typical form of mechanism diagrams in cell biology. This typical form, unlike Figure 5.27 that obviously unites information and the representations from different disciplines, integrates a greater diversity of information from different research areas. Normally, multiple perspectives are integrated at multiple levels. In Figure 5.28, For example, the lipid bilayer structure of cellular membranes, the cristae of mitochondria, and the phosphorylation process of c-jun protein are discoveries by different research projects in different historical periods. They were not discovered for the purpose of establishing a cohesive explanatory model like this. Instead, they are extracted from their original fields and integrated in this specific context, namely, a context of explaining the roles of COX-2 (cyclooxygenase-2) in apoptosis. The components of this model embrace very different levels and scales of space, time, entity, and activity. For the purpose of inter-level and inter-scale integration, the scales of component entities and component activities are not accurately represented but schematised. Neither the length of the arrows nor the distance between the icons necessarily represents the actual temporal and spatial relations between these entities and activities.

Such a mingling of visual elements in mechanism diagrams (eg. Figure 5.28) embodies the practice of building mechanistic explanations. In this sense, mechanism diagrams are simultaneously (1) the representations of explanations and (2) the material embodiments of practice of developing the explanations. A typical mechanism diagram like Figure 5.28 is able to represent how the diverse explanatory schemes are collected and then mapped onto one another. Such processes are required for the formation of a useful explanation for a specific phenomenon, as discussed by Craver and Darden (2013). They term the sources of existing discoveries a “store” of established explanatory schemas (2013, 67). To briefly summarise the processes, the “store” offers different schemas that can serve as candidates for the components of the mechanism of interest (71). The schema can be about activities, relationships, entities etc. Normally, scientists do not simply mix existing schemas together to develop new schemas but assemble existing schemas through long process of retrieval, mapping, adjustment, as well as evaluation and testing of the developing explanations. More importantly, the assembly of new mechanistic models involves not only discovering new parts but also putting “together old parts... in new ways” (2013, 75). In the case of Figure 5.28, many component pathways are existing discoveries, including the pathway of activating COX-2 through phosphorylation of c-jun by JNK2, the disruption of mitochondria integrity, and caspase-9 activation. The stored schemas (in Craver and Darden's vocabulary) for understanding the activities are extracted from these discoveries, including phosphorylation, enhancement of expression, cleavage, and negative feedback regulation. Through employing these “old parts” and adjusting them with experimental results, the authors assemble a new model to explain how shear stress induces apoptosis of chondrocytes. The model encompasses all the employed discoveries and schemas in new ways. The integration of the schemas does not merely mixes them but turns them into compatible components of the mechanistic model.

Biologists are trained to read the synthesis of multi-perspectivity in mechanism diagrams, especially

given the extensive diversity of research fields in contemporary time. They at the same time appreciate the existence of integrative practice required for developing the models represented by the diagrams. The component parts may be familiar to the viewer, while the model as a whole is novel. The integration of different perspectives are represented by different packets of the component information. While some of the component information may be visually simplified or taken for granted (as visually black-boxed), the perspectives are not reduced but can be read by the trained reader. Such integration results in new meanings. Hence the process is a kind of synthesis, just like chemical synthesis of new compounds through using existing ingredients.

The synthesis of heterogeneous perspectives from diverse research interests is just the first layer of the synthetic nature of diagrams. Nonetheless, it is the layer most directly and obviously reflecting the practice of investigating mechanisms. In fact, as previous sections (especially Section 5.3.2 and 5.3.3) have revealed, the process of making mechanism diagrams is sometimes a part of reasoning about the mechanisms. The development of visual languages of mechanism diagrams cannot be disentangled from the development of the mechanistic models. When the trained reader interprets the heterogeneity of the information, the heterogeneity of practice embedded can also be read. The latter is usually taken for granted, not because it is not true but because cell biologists are too used to the inter-field interaction required for model-building.

### 5.5.2 Heterogeneous signs

This section argues that components of mechanism diagrams can have different “sign functions”<sup>107</sup>. The heterogeneity of visual elements in mechanism diagrams is not only due to the heterogeneity of information represented but also because the elements are in their nature different *signs*. Because the complexity of mechanistic explanations for biological phenomena cannot be captured by using only one kind of signs, component elements of mechanism diagrams are heterogeneous in terms of meanings and sign functions. If a mechanism diagram contains only icons of the component entities, it says nothing about either the dynamics or the relationships between these entities. For example, indexical arrows have to be used to represent the directions of physiochemical reactions. Diagrams composed of uniform and single sign functions are not capable of representing mechanisms. In practice, such variety of sign functions tends to be great. It seems not radical for this study to assume that mechanism diagrams must rely on heterogeneous signs.

A comparison between Figure 5.29A and 5.29B shows two aspects of heterogeneity of visual elements, contrasting the heterogeneity of *appearance* with the heterogeneity of *sign function*. Both diagrams are mechanism diagrams, where Figure 5.29B has a typical composition, and Figure 5.29A has a relatively rare composition. Apart from some differences in the acting substances of apoptosis-induction, the narratives in these two diagrams are very similar. In Chapter Four, a comparison between them was used to show the author's creativity in visualisation. Here, two more implications are drawn from the comparison. Firstly, deviations from typical styles and compositions suggest that scientists sometimes experiment on their visual language via abandoning traditional, wide-accepted formats and creating new ones. Secondly, while the visual elements in these two diagrams are both heterogeneous signs, Figure 5.29A serves as a better demonstration of the diversity of sign function due to its uniform style of visual elements.

Experiments on visual language of mechanism diagrams can be about creating new structures of storytelling (which is like the *syntax* of verbal language) or new forms of visual elements (which is like the *vocabulary* of verbal language). Figure 5.29A uses quite basic visual elements and yet arranges them in a creative visual syntax. By contrast, Figure 5.29B creates new forms of the visual elements (new vocabulary), while employing a traditional syntax. Figure 5.29B multiplies the

<sup>107</sup> In Wood's sense. See below and Section 2.5.2.

variety of component signs mainly by creating new appearances for individual packets of information (entity, activity etc.), and 5.29A multiplies the variety of component signs by imparting diverse meanings to uniform elements.

In Figure 5.29B, different component entities and activities are represented by visual elements with different appearances. The entities (the substances) are represented by various colour icons, the downstream events (such as “cleavage of substrates”) and two different physiological conditions (presence and absence of trophic factor) are symbolised by words. Meanwhile, arrows with plural meanings (as discussed in Section 5.3.3) respectively represent indications, sequences, actions, and causalities. The heterogeneity of visual elements in this diagram can be told by their diverse appearances. Different molecules are also represented by different icons. Some of them resemble the actual objects, though in a highly simplified way. This kind includes the trophic factor receptor, the channels across mitochondrial membranes formed by Bcl-2 homodimers, and the apoptosome complex (in the lower left part). In sum, the heterogeneity of component information in this diagram is mirrored in the heterogeneous appearances of the visual elements.

Figure 5.29A unifies the style of visual elements, without reducing but emphasising the heterogeneity of sign function. The distinction between entities and events is blurred by an overlapping use of style. Words are used to represent both entities and events, and squares are also used to outline both entities (eg. “BCL-2/BCL-X”) and events (eg. “cytochrome c release”). Some of the word-symbolised objects have no outlining (eg. “14-3-3 dimer”). In short, there seems to be no consistent rule for the visual elements. The meanings of arrows and stop signs are as plural as observed in many mechanism diagrams. Therefore, the signifying function of each visual element has to be individually read via careful interpretation of the meanings. Sometimes the sign function is iconic, when a word (symbolic) is outlined by a square and the two elements are jointed to make a single icon of a molecule. Sometimes the sign function is indexical, when an arrow points to the route of “cytochrome c release leading to caspase-3 activation”. In this diagram, the elements are heterogeneous *not* because they are visually distinguished, which is the case of Figure 5.29B. They are heterogeneous because of their different signifying functions and epistemic roles in this visual narrative, despite their uniform style.

Biological mechanisms are too complex to be visualised by using homogeneous kinds of signs. Heterogeneity of both sign functions and appearances of visual elements is seen in most (if not all) biological mechanism diagrams. Even uniformly designed visual elements can possess highly diverse sign functions.

### 5.5.3 Data-diagram inter-referencing

This section discusses a special way of composing and reading diagrams: inter-referencing. This kind is roughly characterised by its feature of uniting data images (such as photographs, usually without changing them) and diagrams. This section will raise two points. Firstly, a synthesis of data images and diagrams acts more than pairing them but producing novel relationships between them. The relationships are usually more than simply one-way transformation from photographs to diagrams. This is against Lynch's general assumption that biological diagrams are one-way transformative renderings from photographs (1990, 160, reviewed by Section 2.6 of this thesis). This section will argue that, within new contexts created by the synthesis, data images and diagrams mean different things to each other but not merely sequential renderings. Secondly, a synthesis of data images and diagrams makes them both visual components of the wholes. The data images gain new sign functions and new epistemic roles, which are different from the original contexts of data production.

A special pattern of reading is required for interpreting the messages of such special kind of data-diagram unities. Chapter Four has termed this special reading pattern *inter-referencing*, for the reader interprets the data images whilst referencing to the diagrams, and vice versa. Normally, data images and diagrams are treated as two different kinds of imagery by the scientists, in terms of the rules of production and the limitation of manipulating. In scientific papers, these two kinds of images tend to be separately numbered. However, the inter-referencing uniting of data and diagrams crosses the boundary between them. In such a case, different kinds of research images can be turned into a coherent vocabulary of new visual narratives.

Inter-referencing can render new sign functions and new epistemic roles of the component images. The new functions and roles are activated in the new contexts of the united wholes. Figure 5.30 and 5.31 present two different kinds of diagram-photograph unity, where the relationships between the data images and the diagrams are different. Yet both examples employ the data images and diagrams as visual components of the new wholes. Neither case can be considered as simply a combination of transformative renderings (diagrams) and their sources (photographs). Figure 5.30 turns the photograph into an icon for a cell event in the model. Figure 5.31 joints data images with diagrams, showing the transformation and translation of ideas into different kinds of visualisation. Figure 5.31 requires the viewer's eye to swing between its constituent parts, where the schematic model and the experimental images not only independently convey research findings but also speak for each other's epistemic role.

The use of data image in Figure 5.30 is about deploying an indexical function of the photograph (in the context of laboratory activity) and turning it into an iconic function in the new context of meaning. The new context is formed specifically in this mechanism diagram of apoptotic progress. The details of this diagram have been described in Section 4.2.6. The experimental image on the right end is an electrophoresis photograph of “DNA laddering”, which is an experimentally produced representation of fragmented DNA. In apoptosis research, such fragmentation is viewed as a “hallmark” feature of apoptotic progress. When scientists observe DNA laddering, the evidence is nearly sufficient for claiming that the cell is dying (though in practice, evidence obtained via other approaches is required). Thus from the experimental aspect, DNA laddering is an *index* to apoptosis. However, in this diagram, the signifying function of this DNA laddering photograph tends to be *iconic*. Through using this photograph as a visual component, this diagram makes use of the indexical feature of “DNA laddering” and then converts the photograph to an icon for apoptosis. When this electrophoresis photograph is seen in the lab, it functions as an index to apoptosis occurring in certain tangible cells. When it is seen in this diagram, it no longer points to the physical occurrence of apoptosis but *stands for* apoptosis per se. Interestingly, there is a group of words beneath the photograph: “internucleosomal DNA cleavage–apoptosis”. This word group is aligned with the other word groups that describe other stages of progressive change. That is, this word group alone is enough to symbolise apoptosis. Either the photograph of DNA laddering or this word group could be removed, without affecting the conveyance of ideas. Their coexistence reinforces the iconic function of the photograph of DNA laddering. In sum, this experimental image is employed as an iconic component of the model. This new sign function only works in the context formed through uniting the schematic drawing and the DNA image.

Figure 5.31 contains three layers of messages connected to each other via two stages of transformation and translation of ideas. Each layer has two-way connections with its prior and following layers. This diagram as a whole exhibits a visual consistency in terms of both the use of colours and the alignment of the component images. In other words, the signifying system throughout the three layers of messages is coherent. Based on this system, the inter-referencing interpretation between these layers makes sense. Section 4.2.7 has detailed both the meanings of each part of this diagram, as well as the meanings that only emerge through an inter-referencing reading pattern. The first stage of connection is between the fluorescence in the photographs (the



first-layer message) and the chart graph of the change in fluorescent intensity (the second-layer message). The second stage of connection is between the data in the chart graph and the schematic model (the third-layer message). Some of the colours (red and green) used in the experiment are the same with the colours used in both the chart and the schematic model. It is important that the symbolic meanings of these colours in different parts of the diagram are intentionally consistent (see Section 4.2.7). The red colour always signifies the pre-apoptotic phase, and the green colour always signifies apoptotic phase. The blue colour seen in the lower photograph comes from a specific dye for cell nuclei. It simply marks the locations of cell nuclei and does not apply to the system of colouration. Despite this, the arrangement of the lower photograph is consistent with the signifying system in a different manner. In this diagram as a whole, the loci of apoptosis are always on the right side. Since cell nuclear condensation is a hallmark feature of apoptotic cell, the shrinkage of blue colour in the right terminals of the nematodes visualises the “apoptotic zone” of the organisms. This “apoptotic zone” is in line with the green colour visualising the apoptotic zone in the upper photograph.

Considering Figure 5.31 as a coherent visual narrative of apoptotic mechanisms, it employs three different kinds of research images (photograph, chart graph, model diagram), where each has its own vocabulary<sup>108</sup>. A specific syntax (formed only in this context) unites them and gives new epistemic roles to them. When the two photographs enter this new context of meaning, they serve to display the roles of certain genes in progressive phases of apoptosis. These phases are firstly visualised by the photographs, secondly translated to quantitative data (visualised by the chart graph), and eventually explained by the model diagram. The chart graph enters this new context of meaning and becomes the background for the mechanistic model. The viewer has to inter-reference between these three vocabularies and read them both separately and conjointly. The interpretation of the whole is accomplished by both recognising the phenomena and understanding the explanation. Similar to other mechanism diagrams, the ultimate purpose of this diagram is to provide an explanatory model for the phenomena observed in the experiment. Yet this special composition at the same time displays what the model is explanatory for. Moreover, the use of the chart graph in the middle shows exactly how the explanations are developed through layers of translation and transformation. This diagram as a whole visualises the reasoning process from experimentation to explanation. This visualisation of the reasoning practice rises from the coherent uniting of three visual vocabularies within one specific syntax. This is to say that the composition of Figure 5.31 visualises simultaneously the ideas and the development of the ideas.

Examples raised in this section confirm the role of diagrams in developing biological mechanistic models. Some studies of biological mechanism research<sup>109</sup> suggest that the making of diagrams can be a part of thinking process. Authors studying other sciences also argue that conceptualisation in some sciences and technology rely heavily on visual thinking<sup>110</sup>. The term “thinking” in various sciences is a rough collection of research activities that may refer to hypothesising, evaluating, theorising, adjusting previous hypotheses, predicting etc. Figure 5.15 has already presented two examples of the epistemic roles of visualisation in reasoning about biological concepts. In terms of the way visualisation participates in the reasoning, Figure 5.15 and 5.31 are very different from each other. Figure 5.15 works through visual analogy. Figure 5.31 works through rendering new

<sup>108</sup> In the literature of history and philosophy of science, while the classification of scientific images slightly varies by the author, some classifying criteria are basically similar. This similarity seems to result from the common way scientists treat their images. Photographs, graphs charts, and diagrams are normally in the “figure” family and then classified into different subfamilies.

For example, in Gross et al. (2002), scientific visual objects (in this study: visual items/VI) are classified into several types: tables, graphs, schematics, and realistic renderings (largely photographs). Their schematics are similar to the diagrams in this study. The realistic renderings include drawings of microscopic pictures, which in this study are categorised as object diagrams.

<sup>109</sup> Bechtel, 2006; Craver and Darden, 2013. See Section 2.4.

<sup>110</sup> Rudwick, 1976; Ferguson, 1977. See Section 2.2.

epistemic roles of different kinds of research images and making them speak for one other. But they both demonstrate that visualisations used in the reasoning process of biology can creatively synthesise different iconographic resources. Furthermore, Figure 5.30 and 5.31 show that the relationships between data images and diagrams are varied and can be changed according to the syntaxes of visual narratives.

This variety of relationships between data images and diagrams has gone far beyond Lynch's thesis on the transformation from photographs to diagrams (see Section 2.6). Images composed of both data images and diagrams (such as Figure 5.30 and 5.31) on the one hand serve the epistemic role of Lynch's transformative diagrams. On the other hand, importantly, the component data images gain new signifying functions and new epistemic roles in the new contexts formed in such inter-referencing constructs. The epistemic roles of the photographs in Figure 5.30 and 5.31 are no longer limited to the sources of transformative renderings. In Lynch's argument, the diagram is like an upgraded version of the photograph, in terms of the power of asserting ideas. Lynch tends to treat diagrams as either direct or indirect derives (renderings) from photographs, without recognising the versatile roles of visual items in biological visual narratives. In practice, photographs can be components of diagrams, and their signifying functions may be changed.

The gap between Lynch's viewpoint for biological diagrams and the actual richness of diagrams may have resulted from the time difference between his thesis (the late 1980s) and the period surveyed by this study (circa the 1980s till the 2000s). Traditionally, biological illustrations had long been about drawings derived from observations (via either instrument or naked eye). But iconographic resources for diagram-making have drastically expanded in recent decades. This is plausibly a result of the rapid growth of complexity of ideas (as exemplified in previous sections of this chapter). The quantitative results of this study have shown that object and mechanism diagrams are equally prevalent, where the prevalence of mechanism type grows in some journals. The mechanism type—as a diagram type with most richness in meanings and most openness to creative styles—can embrace not only the other diagram types but also data images. As this type grows its coverage, it evolves to employ data images in novel ways. The data images can now be the icons for biological events, the indices to biological phenomena, and parts of explanatory models.

In conclusion, research images are versatile in terms of both signifying functions and epistemic roles. This versatility, just like the versatility of other visual elements (as discussed in previous sections), is closely related to the increasingly complex ideas. The functions and meanings of research images (be they photographs, chart graphs, or diagrams) depend upon their *relationships* with other components of visual narratives. The exact and deep meanings of the visual vocabulary vary with the syntax, within which they are given new relationships with one another. Section 5.6 will discuss the importance of building relationships between visual components in biological mechanism diagrams. The generated array of relationships as a whole is empowered to assert ideas and mediate intervention, while the components alone cannot.

#### 5.5.4 Supra-perspectives

Some mechanism diagrams contain extra perspectives, which can serve to present higher levels of manipulation and conceptualisation. Such kind of perspective is not made of the components within the model mechanisms but a novel one emerging from the synthesis of the previously discussed components. Thus this study terms it *supra-perspective*. Previous sections have argued that mechanism diagrams can be a part of reasoning processes. The use of supra-perspectives tends to visualise the process more explicitly. Some supra-perspectives represent the author's treatment of the components of the models, eg. categorisation of entities or sequencing of events. Some represent the author's treatment of the relationship between the research process and the discovery.

In sum, supra-perspectives normally represent a comprehensive view of the heterogeneous information synthesised in cell models. Therefore, visual elements of supra-perspectives are generally drawn outside of the cell model.

Figure 5.32 embodies the synthetic and heterogeneous features of mechanism diagrams to a greater extent than most of previous cases, for it synthesises both the component perspectives of the explanatory model and two supra-perspectives. These two supra-perspectives are added to the cell model from outside, both visually and conceptually. They have an explicitly asserting function to show the reader how the author treats the component information of this model. In the upper and right margins of the diagram, two groups of sign respectively represent two different perspectives: the upper group are verbal descriptions of two pathways (“transcriptional induction of glucose utilization” and “transcriptional repression of fatty acid utilization”); the right group contains words and lines describing three layers of reactions occurring within the cell. While they both classify the events in the cell model, they have different viewpoints. The upper group classifies the events in terms of biochemical consequences (ie. induction or repression, as well as utilisation of glucose or fatty acid). The right group classifies the events in terms of location (ie. cytosol, intermembranal space of mitochondria, and mitochondrial matrix). In other words, these two supra-perspectives on the one hand differ from the component perspectives within the model (such as the Acyl-CoA chain reactions), and on the other differ from each other because they represent different treatments of the components.

The synthesis of heterogeneity in Figure 5.32 is further seen in the visual connection between conceptual and physical spaces. As the two supra-perspectives partition the space of the model, the divided space at the same time represents several kinds of cellular spaces. The cellular spaces include: (1) the space divided by cell membrane and the double membranes of the mitochondria and (2) the loci of two different biochemical pathways (ie. the two kinds of nutrient utilisation). Here, the use of blank space simultaneously connects and separates all these conceptual and physical spaces. A few previous cases have shown such use of blank space (see Section 2.5.1 for art history discussion of blank space), but the blank space in Figure 5.32 goes farther by integrating different schemes of thinking. The space inside the model represents physicality, and the space outside the model represents abstract ideas. The viewpoints of the supra-perspectives are not in the physical space outside the cell (albeit visually so) but an abstract space that is not at the same level with the cell. The cell drawn in this diagram represents a physical space for the mechanisms, wherein the component signs represent physical entities and activities. The words within the cell model, such as “Acyl-CoA” and “Pyruvate”, represent the ontological status of these biochemical compounds. But the words outside the cell model (eg. “FA mitochondrial import”) have different meanings. They speak for an intended classification by the author. There are already multiple perspectives integrated within the model (eg. a biochemical perspective studying the metabolic pathways, and a cell transport perspective studying the import activities of glucose). Thus the inclusion of two supra-perspectives brings this synthesis of heterogeneity to a higher level.

Time axes in mechanism diagrams generally function as supra-perspectives. The two diagrams in Figure 5.33 contain time axes that both serve as the references for reading sequential events, yet with slightly different roles in the narratives. In Figure 5.33A, the time axis places a scale for charting the activities within the mechanism (NGF inhibits cell death). In Figure 5.33B, the time axis is correlated with both experimental design and experimental results. This diagram, as discussed in Section 4.6, integrates three diagram types: experimental design, mechanism, and experimental result (which is categorised as “other” type in this study, see Chapter Three). Apart from being a reference of timing, the time axis in Figure 5.33B contributes to making the diagram as a whole a genuine visualisation of explanatory model, instead of being a mere display of interventions and consequences.

The key contribution of the time axis in Figure 5.33B is integrating descriptive and explanatory

accounts. The trained eye can interpret from a superficial layer on description to a deep layer on explanation. Here I explain this two-layer interpretation with two examples of arrows (as supra-perspectives). The background is that, due to the lack of explicit representations of causality, Figure 5.33B might appear merely as a chronology of cell events. Figure 5.33A represents causality in a more explicit way by displaying a series of substances (proteins and biochemical compounds) on the top of the diagram. This series explains the sequential events stage by stage. Nonetheless, in Figure 5.33B, no explanation is explicitly visualised. The arrows that link the events seemingly point to the directions of sequential events. But the deeper message of these arrows is really about causality. The first example is the arrow linking “SAMC” (a chemical) and “inhibition of MT dynamics” (where MT stands for microtubule, a kind of cell skeleton). It has twofold meanings. Firstly, it represents the treatment on the cell by SAMC, as it passes through the twin lines that represent the bilayer of cell membrane. Secondly and implicitly, it represents a causality the author concludes from the experiment, ie. SAMC “*causes*” (Xiao et al. 2003, 6828-9) depolymerization of microtubules and thus loss of dynamics of microtubules. The second example is the arrow linking “inhibition of MT dynamics” and “JNK1 activation”. This arrow has a chronological function, showing that the inhibition of MT dynamics occurs prior to JNK1 activation. This temporal relationship can be clearly told by referencing to the time axis. Meanwhile, this arrow has a deeper meaning: a causal relationship concluded from the experiment. This causality is proven in both indirect and direct senses, where each sense contains more than one way of reasoning<sup>111</sup>. The informed viewer decodes these multiple meanings of the arrows.

The use of supra-perspective makes this model both descriptive and explanatory. Borrowing Craver and Darden's metaphor (2013, see Section 2.4 of this thesis), the reading process through the layers of the arrow meanings is like going from a “black box” to a “glass box”, when the explanatory details of the mechanism are gradually revealed. The time axis in Figure 5.33B is a reminder of the importance of the experimental design, showing the overlap between temporal and causal relationships between the events. The part beneath the cell membrane could be a model on its own, while the whole model is completed by adding a supra-perspective, ie. the time axis. This supra-perspective maps three different schemes of thinking onto one another: the experimental design, the descriptions of sequential events, and explanations for the events.

### 5.5.5 Conclusion: rise of supersigns

The previous subsections have discussed four layers of the synthetic nature of mechanism diagrams. The heterogeneity embedded in mechanism diagrams is seen in these aspects: the information represented, the sign functions of visual elements, special inter-referencing unites of data images and diagrams, and supra-perspectives. The next section will explore how synthesis of heterogeneity generates meanings of mechanism diagrams as wholes. Such meanings cannot be produced when any of the components are present *alone and separately*. I shall show that the synthetic features of biological mechanism diagrams resonate with the synthetic features of maps<sup>112</sup>. This leads to my treatment of mechanism diagrams as “supersigns”.

## 5.6 The power of mechanism diagrams

<sup>111</sup> In the indirect sense, the removal of JNK1 action—via (a) use of JNK1 inhibitor and (b) transfection that inactivates the gene—counteracts the effect of SAMC on microtubules. In the direct sense, an induction effect of SAMC on JNK1 activation is observed. Thus it is concluded that JNK1 activation simultaneously (1) mediates the pathway of SAMC effect on the MT and (2) is an effect of SAMC treatment on the cell.

<sup>112</sup> Wood, 1992; 2010.

This section will argue for the asserting and engaging power of mechanism diagrams as supersigns. Section 5.6.1 introduces the notion of supersign imported from cartography (see Section 2.5.2) and previews how I will develop my arguments on the asserting and engaging power of mechanism diagrams. This chapter shall close with a comparison between two kinds of supersigns: biological mechanism diagrams and maps.

### 5.6.1 Mechanism diagrams are supersigns

This section argues that biological mechanism diagrams can be viewed as powerful “supersigns”<sup>113</sup>. This section shall discuss that the power of mechanism diagrams as supersigns is twofold: assertive and engaging.

Section 5.6.2 argues that mechanism diagrams have the power to assert ideas. They are synthetic diagrams composed of heterogeneous components. Thereby they become assertive in conveying ideas that only exist in the contexts formed through constructing the components in specific syntaxes. This happens via building special relationships amongst the visual components. As argued in previous sections, a biological mechanism diagram is an image as a whole that synthesises heterogeneity of both sign functions and the perspectives embedded in the signs. Because of the nature of biological mechanism research, and because of the reflection of such nature in the visualisation, both the layers and levels of constituent information are multiple and integrated. Meanwhile, the constituent signs are representations of dissimilar things (as argued by Bender and Marrinan, 2010), but they gain new meanings within the new relationships with other constituent signs in the diagrams. *Mechanism diagrams are about relationships*. I put this argument in the form of imitating a quote of Wood's (1992): “maps are about relationships.”(132; 139). It is the syntactic relationships amongst the visual elements that form the relative meanings of visual element.

Section 5.6.3 argues that mechanism diagrams are pragmatically powerful, for they are capable of facilitating real-world intervention in the mechanisms. This happens via engaging the viewer in the process of meaning generation. Mechanism diagrams are powerful in provoking dialogues between the viewer and the community of interrelated (or collaborative) researchers. The viewer, who is usually a practitioner, finds their connection with remote practices through actively interpreting the constituent relationships built in the diagrams. The viewer is thereby engaged in the collaborative web of mechanism research. Such connections are especially important in the research process of complex, multi-level modelling that requires interaction amongst different perspectives. As reiterated throughout this study, mechanism diagrams embody the interaction amongst different perspectives of mechanism research. In this sense, mechanism diagrams serve as the maps for the practitioners to explore within the array of discoveries. As the viewer investigates biological mechanisms in order to intervene in them (as argued by Craver and Darden, see Section 2.4 of this thesis), mechanism diagrams play a role in mediating between the formation of ideas and the action of intervening.

Section 5.6.4 explicitly suggests an analogy between biological mechanism diagrams and maps. This analogy comes from the feature of mechanism diagrams that they are the embodiments of the interwoven processes of image-making and reality-exploring. This feature is comparable to a cartographic notion that maps are simultaneously the representation and the practice. Previous sections have shown the intimacy between practice and representation in biological mechanism research. The making and re-making of mechanism diagrams are part of the practice of constructing explanatory models. Section 5.6.4 will step further by arguing that mechanism diagrams, like maps,

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<sup>113</sup> My extension of the notion “supersign” is based on a combination of cartography (Wood, 1992), art history (Bender and Marrinan, 2010), and philosophy of science (Gooding, 1990; Craver and Darden, 2013).

are constantly in a “state of becoming” (Del Casino and Hanna, 2005, 36). The constant interactions between individual researchers and the community, as well as between different stages of theory-development by the same researcher, lead to the constant making and re-making of *both* the models and the diagrams. This echoes with some cartographers’ argument that “maps and territory are co-constructed” (Dodge, Kitchin and Perkins 1999, 18, as introducing Corner, 1999). Mechanistic explanations for cell phenomena are continually co-constructed and co-changed with their visual representations.

### 5.6.2 Power of asserting ideas

Biological mechanism diagrams studied in this thesis exhibit the features of “supersigns” and are capable of asserting ideas. Such features come from the relationships built amongst the synthesised components (normally heterogeneous). The visual grammar is a salient factor in generating new meanings of both the component signs and the whole.

I imported the term “supersign” (a construct of synthesised signs) from Wood’s cartographic work (see Section 2.5.2 of this thesis), as biological mechanism diagrams are comparable to maps in three ways. Firstly, some components of cell models can be analogised to geography, both visually and functionally. For example, the blood vessels are comparable to canal systems. Cellular compartments are also frequently analogised to geographical landscapes. “Cellular landscapes” as a phrase is easily found in scientific literature, either within specialist community or in the general public<sup>114</sup>. Along with this phrase, “navigate” is a commonly used verb to describe the action of seeing around in cell image. Secondly, mechanism diagrams compact information of these biological “landscapes” and their relationships, just like maps compact information of geographical landscapes. Thirdly and most importantly, mechanism diagrams build new relationships between their heterogeneous component signs within specific syntaxes. Through such synthesis, the wholes are able to assert new, original meanings.

Visual elements of mechanism diagrams—words, arrows, geometric shapes, depictions of special objects, or blank space—are made have new relationships with each other within a specific configuration. Configuration of visual elements functions as the scaffolding of visual narratives. This important role of configuration is due to the heterogeneity and versatility of component signs. Examples raised previously have demonstrated the heterogeneity of both perspectives and signs integrated in mechanism diagrams. Meanwhile, it has been shown that component signs of biological diagrams can have plural meanings in different contexts of use. Therefore, building specific relationships amongst the components is key to meaningful integration of such versatile signs.

The configuration of elements in visual language can be compared to the syntax of verbal language. It follows some “visual grammatical rules”. Such rules are required for effectively and productively transferring ideas across different research cultures. As seen in the aforementioned cases, there are some common visual grammatical rules of biological mechanism diagrams. The cases have also shown that, despite the rapidly advanced graphic technologies, certain grammatical traditions for visualising mechanisms are still in active use. This study has shown that creative experiments on compositions (which can be viewed as novel grammar) tend to remain rare. This suggests that not only the forms of visual elements but also the ways they are correlated to each other have some conventions (but not necessarily standardised). The social implication of the acceptance of different “grammatical rules” is clear. Visual communication usually needs to employ some conventions so

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<sup>114</sup> For example, *Navigating the Cellular Landscape with New Optical Probes*, <http://videocast.nih.gov/summary.asp?Live=12338&bhcp=1> (NIH Center for Information Technology, National Institutes of Health, 2013)

that the narratives can be understood by wider specialist communities. Since the middle to late twentieth century, biological sciences have become so large-scale that distributed research institutions are increasingly solving enormous “puzzles”<sup>115</sup> in a collaborative manner. This is especially obvious in mechanism research. Given both the geographical distance and the cultural difference between research institutions, information is meant to be greatly distributed, too. Visual formats of communicating are a part of scientific arguments and have relatively low barriers to users of different languages. Thus visual communications are deemed to effectively and rapidly transmit messages across different cultural settings. Visual communicating process must minimise possible signal loss during transmission, where plurality of interpretation can lead to loss or misreading of the signal. This requires the visual grammar to configure the elements in conventional syntactic structures. Conventional grammar of diagrams ensures the interpretation by different viewers to be within an agreed range of meanings.

Visual syntax is thus the salient factor in generating new meanings through correlating visual elements with one another. Component visual elements of mechanism diagrams are heterogeneous sign systems that can have plural meanings in different contexts of use. Especially, some basic elements (such as arrows and geometric shapes) are so universally used in various contexts that their meanings (as single signs) are unlikely to be told without their relationships with other signs. Normally, the meanings of such general signs are assessed and recognised when they form meaningful constructs together with other signs. Such constructs can be studied with the notion of “syntactical products” (Wood 1992, 134)<sup>116</sup>. For example, in Figure 5.25B, the black line and the colouration beneath it together signify “plasma membrane” along with the existence of other signs such as:

- ⤴ the words “plasma membrane” and an indicative line (the most direct expression of the meaning);
- ⤴ the icons for mitochondria and the reactions centring on it (pointing out where intracellular space is);
- ⤴ the words “death receptor” and “death receptor ligation”, as well as the arrow indicating the direction of pathway (pointing from extracellular to intracellular).

The black line and the underlying colouration together form syntactical constructs with the above signs. Thereby they become an icon for the plasma membrane, in terms of both existence and location. This iconic meaning has to be interpreted in the grammatical context of this diagram specifically. This is comparable to the case of distinguishing between icons of rivers and highways on maps against other syntactical constructs in the background. The semantic impressions of the icons alone are not really useful in making this distinction:

We attend more to the syntax of the system than the semantic import of its components. We don't distinguish blue highways from rivers because their signifiers are a little wider and a little less sinuous, but because they are structured differently as systems, because they are manifestly different landscapes. (Wood 1992, 138)

Every constituent sign of the mechanism diagram becomes meaningful when assessed against the meanings of other signs. In Figure 5.25B, the gradient coloration of light green in the background is not just a background for painting but the icon of cytoplasm. This is comparable to Wood's example that a white space on the map is not “an insignificant white surface” but “Illinois or Texas” (140). In both cases, the syntactical structures of visual elements play the key role in producing specific meanings of both the elements and the wholes. Here, the difference between these biological

<sup>115</sup> Section 3.3.3 clarified that, in this field, this is a common metaphor and not necessarily in Kuhn's sense.

<sup>116</sup> In Wood's example, if a sign is made “conjugated with another”, the conjugated two should be viewed together as an “elemental construct” that is accommodated by the map (the whole).

diagrams and maps lies in the display of temporal course. Mechanism diagrams normally represent dynamic relationships composed of multi-layered spaces and times. Maps tend to emphasis the spatial relationships (with occasional exceptions that some thematic maps narrate dynamic processes).

New and original relationships built by specific syntaxes leads to the formation of original narratives. Mechanism diagrams assert new ideas that do not appear in separate signs but are generated from the signs being configured in the syntaxes of the wholes. In this sense, biological mechanism diagrams and maps are comparable synthetic supersigns. Wood (1992, 2010) refers to this power of maps as “presentational” but not “representational”, due to the originality of ideas conveyed by maps (as supersigns). Wood's terminology can be compared to Daston and Galison's discussion of the transition of new images from representation to presentation. New images produced during the process of intervention are presentations rather than representations, they maintain, partly because such “new images” are generated for the first time by the active user to present one's original ideas to others<sup>117</sup>. Following these two sources, this study argues that biological mechanism diagrams are produced by the researcher, who is simultaneously the user and the viewer, to assert original ideas emerging from the new component relationships. Such assertive power of mechanism diagrams results from their similar features to maps. Both maps and mechanism diagrams are about integrating heterogeneous sign systems. Through the integration, new and multi-layered relationships amongst the signs are established. Both maps and mechanism diagrams inform the viewer about new meanings, which must be assessed via reading the component relationships within special syntactical frameworks.

### 5.6.3 Power of doing work

Biological mechanism diagrams as synthetic supersigns play a role in real-world practice. This section discusses the ability of mechanism diagrams to take part in mediating the intervention in biological mechanisms through provoking dialogues. The dialogues take place between: (1) the viewer (researcher) and the research community, and (2) different stages of model developing by the same researcher<sup>118</sup>. In this sense, the research dynamics—the continual interactions between different perspectives and different stages of developing a perspective—is embodied by the mechanism diagrams. This is to say that visualisation of mechanisms has a role in the pragmatic value of biological mechanism research (see Section 2.4). Because interaction is crucial in the research culture, and because mechanism research has a purpose to intervene in the physical processes, mechanism diagrams have the power to mediate real-world practice via serving as platforms for interaction.

Diagrams are capable of engaging the viewer in a meaning-generating dialogue. This comes from the above-argued requirement for the viewer actively interpreting the new relationships between the component signs. Bender and Marrinan argue that (2010, see Section 2.5.2 of this thesis), in addition to the correlation amongst heterogeneous visual elements (or sign functions, in Wood's language) within the diagrams, the viewer is also “correlated” with the diagrams. In the case of art history, the meanings of the diagrams are generated when the viewer's personal experience and private affection are evoked by the image. In the case of biological diagrams, the correlation between the viewer and the diagrams is about employing professional knowledge to decode the

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<sup>117</sup> For their reasons to treat new images as presentations, see Section 2.1.2.

<sup>118</sup> When referring to individual researchers and viewers, this thesis sometimes uses singular nouns. This is not to say that contemporary biological research can be conducted by single individuals. In fact, the basic “unit” of individual doing research is usually a laboratory team. The occasional use of singular “researcher” and “viewer” in this thesis refers to such a unit.



component signs into intelligible messages and then making *use* of the messages. Bender and Marrinan treat the correlation between art works and the viewer as an engagement of the viewer into an active reading process of the images. Thus the viewer is the reader *and* the user, who actively participates in the meaning-generation process of diagrams. Such an engagement has its resonant parallel in the context of biological diagrams, where the active reading of the meanings also turns the viewer into the reader and the user. In the case of art history, the viewer's projection of personal experience and affection onto the image plays a significant role in the engagement. In the case of biological diagrams, this study argues, the meanings of mechanism diagrams emerge in a comparable yet more complex way.

This way is complex because the dialogues continually involve both space and time. The dialogues between biological mechanism diagrams and the viewer reflect the dynamics of mechanism research. On the one hand, mechanism diagrams are visualisations of the array of discoveries and are thus important to individual researchers' interaction with the wider community. On the other hand, mechanism diagrams are visualisations of the developing models and thus serve to mediate the communication between different stages of development by the same researchers. Therefore, mechanism diagrams play a role in both communication between different perspectives and different times. I have described in Section 2.4 that biological mechanism research engages the user in a circular process of developing theory. This process may include (but is not limited to) the stages of hypothesising, evaluating, experimenting, revising and so forth. During such a cycle, the researchers frequently refer to the array of discoveries and locate their ideas in the broader explanatory models. Meanwhile, the development of explanatory models by the same researchers is comparable to Gooding's argument about construal of physical phenomena (Section 2.3.3), in terms of the researcher's need to communicate with oneself at different times.

Mechanism diagrams are intimately involved in such a research dynamics. This involvement has been suggested by Bechtel's argument on the research process of cell mechanisms (2006). Cases analysed in this study demonstrate that the (re)search of biological mechanisms is greatly intertwined with both the production and the use of diagrams. When the scientists produce diagrams to communicate with their peers in order to obtain collective judgements, they use diagrams to trigger a dialogue between the supersigns and the user. Both the author and their peers can be the user, having dialogues with the meanings of the diagrams based on their research interests. During such dialogues, they map their practices onto the existing knowledge, and vice versa.

In sum, the engaging dialogues take place via two means and are reflective of the dynamics of mechanism research. Firstly, the user (researcher) interacts with peer intellectuals from different settings of practice. That is, different perspectives from distributed places interact with one another through interpreting the meanings of mechanism diagrams. Secondly, the same user (researcher) has a conversation with their own ideas developed at different times, via revisiting and revising the diagrams. Diagrams embody the process of the researcher continually mapping the developing ideas between the past and the present. Thus mechanism diagrams in contemporary biology are the hubs of sharing and exchanging ideas—between different places, times, and perspectives.

Interaction amongst different perspectives is essential for productivity of mechanism research, when the models are developed to be construed by other specialists within the community<sup>119</sup>. Here, mechanism diagrams (as synthetic supersigns) are the visual and material platforms. Section 2.1.1 has maintained that, in contemporary biological practice, the judgement is made collectively through interaction amongst diverse perspectives. Due to the complexity of mechanistic explanations, productive agreements about the models have to be obtained via a collaborative viewpoint for biological phenomena. This is to avoid the domination by a single, specific perspective. Chapter Four and Section 5.5 have shown that mechanism diagrams are visual

<sup>119</sup> This discussion is set in the vein of Gooding's thesis (1990) on the process of construal, which includes: firstly by individual scientists, and secondly by other specialists in the community. See Section 2.2.3.

embodiments of synthesising perspectives, in terms of both information and signs. Thus mechanism diagrams can be considered as the visual embodiments of the interactions amongst the researchers. Diagrams serve as the visual repositories of researchers working collaboratively toward a productive end.

The productive end is to offer grounds for intervention in the mechanisms. Hence biological mechanism diagrams contribute to the pragmatic value of mechanism research. I have discussed in Section 2.1.3 and 2.4 that biological mechanism research is pragmatic and engineering-influenced. Such an ethos of research activity may result from the nature of mechanistic thinking of biological phenomena. The pragmatic purpose to intervene is explicit in biological mechanism research—understanding mechanisms is to find ways to control them. In this regard, visualisations of mechanistic models play a crucial role in supporting this pragmatic value, through mediating the interaction amongst different systems of practice and interest.

In this pragmatic context, researchers of biological mechanisms are engaged in both (1) the growth of mechanistic models and (2) the use of knowledge of the models to produce desired effects. Diagrams facilitate visual reasoning about biological mechanisms, serving as the media for:

- (a) conserving traditions and shedding light on new questions;
- (b) provoking collaborative interest in understanding the causes and producing effects.

In biological mechanism research, diagrams are not just “a part” of scientific argument (as argued by Gross et al., 2002. See Section 5.1), they are a uniquely crucial part. The features of biological mechanisms, eg. multi-level integration and multi-field convergence, are reflected in diagrams. The means they provide the researchers (who come from diverse fields) to collectively perceive and conceptualise the mechanisms is irreplaceable by text. They are the “working objects”<sup>120</sup> in the research process. Through the employment of such working objects, the knowledge conveyed by them and the practice embedded in them are channelled into practical intervention. This is parallel to the power of maps to influence the culture they are simultaneously produced in and representing. Mechanism diagrams are pragmatically powerful in the research culture they simultaneously embody and emerge from.

#### **5.6.4 Comparing diagrams and maps**

Following the discussion on the pragmatic context, this section discusses how mechanism diagrams gain their status of constantly “becoming”. In such a status, the diagrams are simultaneously the representation and the practice. The notion of status of becoming is borrowed from critical cartography<sup>121</sup> and used in this thesis to reveal the important role of diagrams that interweaves the processes of visualisation and model-development. This study argues that such a status of mechanism diagrams emerges in two aspects (as raised in the following paragraph). Both are comparable to the status of becoming of maps. Yet I shall then point out that biological mechanism diagrams are at the same time different from maps, for their characteristics have the potential to transcend the cartographic debates around objectivity and authority.

#### **Similarities**

The first aspect is the historicity of biological diagrams. This results from the previously discussed

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<sup>120</sup> I use this term in the vein of Daston and Galison (2007) and Bender and Marrinan (2010). See Section 2.1 and 2.5.1.

<sup>121</sup> See Section 2.5.2; also see Del Casino and Hanna, 2005.

research processes embodied, and the evolution of visual languages embedded, in the diagrams. As previous sections have reiterated, these processes include continually data-gathering, model-building, error-correcting, as well as inter-field and inter-level interaction and integration between different perspectives. These are constantly-happening construals by both individual researchers and the wider community at different times. The components of mechanism diagrams not only represent the knowns—including entities, activities, and their relationships—but also represent *how* these components have come to be the knowns. The development of the representational codes has its history, too. As this study has shown, the visual conventions are not given but evolved. The trained eye decodes the conventions in the diagrams, and it at the same time decodes the historicity embedded in the making of diagrams. Both the represented (ie. the explanatory models for specific phenomena) and the representations (ie. the encoded visuals) are not fixed in the first place. Instead, they have evolved and are still open to evolution. This aspect resonates with the notion of “maps as practice” argued by cartographers, where the agency of maps:

... lies in neither reproduction nor imposition but rather in uncovering realities previously unseen or unimagined, even across seemingly exhausted grounds. Thus, mapping *unfolds* potential; it re-makes territory over and over again, each time with new and diverse consequences. (Corner, 1999, 213, italics in original)

The coding of the sign systems in maps also parallels biological mechanism diagrams in terms of the professional training of both forming and reading visual conventions:

[But,] map knowledge is never naïvely given. It has to be learned and the mapping codes and skills have to be culturally reproduced so that the map is able to present us with a reality that we recognize and know. (Pickles, 2004, 61)

The second aspect of the “status of becoming” of mechanism diagrams is the deep involvement of the diagrams in the research and intervention processes. Such involvement extends into the future. This aspect cannot be separated from the historicity of the diagrams, for the making and re-making of diagrams are intertwined with the constant process of making and re-making the models. In the sense that mechanism diagrams engaging their users, they (as practice) bring about new problems and activate future research. This study has presented examples of mechanism diagrams integrating the knowns and the unknowns. The unknowns, which are not yet actual, are visualised to await *actualisation* through the users' research activity<sup>122</sup>.

This study has also shown that different models developed by different perspectives can have overlapping interests. In such cases, diagrams play a role in defining the boundary of the models by different local cultures. Again similarly, the mapping practice defines and re-defines the territory from time to time:

Maps are of-the-moment, brought into being through practices... *always* remade every time they are engaged with; mapping is a process of constant re-territorialization. As such maps are transitory and fleeting, being contingent, relational and context-dependent. (Kitchin and Dodge, 2007, 5, italics in original)

In cartography, this defining and re-defining of the territory can embed social, political and cultural interests.

In biology, this study does not cover much social implications but focuses upon the application of Wood's notion of interested selectivity (1992, 1-2). This notion is useful for considering how the above-discussed pragmatic value of mechanism research renders the pragmatic power to mechanism diagrams. Usually, cell biologists visualise an explanatory model for a specific

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<sup>122</sup> Bechtel (2013) has demonstrated this aspect through presenting examples of diagrams containing question marks. My survey includes a lot of similar cases, yet it has discovered some other cases that engage the future design of experiments by using different kinds of visual elements.

phenomenon to present the specific machinery they are intervening in. The link between the pragmatic concern of *controlling* the machinery and both the making and the use of the mechanism diagrams is straightforward. The cases from the journal *Cancer Research* (see Section 4.2.6) especially show that cancer studies tend to specify relatively narrower and shorter pathways than other areas. This is because they are to solve very specific problems in the cancerous process, such as therapeutic effects of a kind of treatment. The pragmatic intention and value of biological mechanism research make the represented models selective. Mechanistic models are in this sense contingencies in the research process. The mechanism diagrams are to represent specific interests in selected perspectives. Instead of being “out there”, the models undergo constant development of their explanatory power. The selective interests are always underlying and reflected in the models. In the context of collaborative mechanism research, such interested selectivity does not undermine the value of the diagrams but reinforces the existence of the above-discussed power of diagrams to assert ideas (see Section 5.6.4.1). This is comparable to the assertive (and sometimes persuasive, see Section 2.1 for Daston and Galison's discussion on images as “presentations”) power of maps, which some cartographers (such as Wood and Pickles) refer to as the discursive power:

[For Wood] the practice of map use is not to send a message, but to bring about a change in the way another person, or group of people, see the world. (Pickles, 2004, 66)

The use of biological mechanism diagrams, moreover, can bring about a change of the ways the other research groups *intervene* in the mechanisms.

## Differences

This section argues that biological mechanism diagrams are still different from maps in the following senses, despite the impressive analogy between maps and biological mechanism diagrams.

Some characteristics of biological mechanism diagrams, on the one hand, make them exempt from the cartographic concerns about objectivity and authority. On the other hand, they may transcend the dichotomy between production and consumption. The cartographic sources cited above contribute to the de-construction of both maps and mapping practice. The call to challenge the neutrality of maps is closely related to the traditional view for the objective and authoritative status of maps. Meanwhile, critical cartography has struggled to deal with the traditionally dichotomised notions of production and consumption, as well as representation and practice<sup>123</sup>. These sources sought to democratise the production of maps, especially in the contemporary context of geographic information system (GIS) and other collaborative devices for mapping. Thus the notion of “maps as both representation and practice” has been novel in the cartographic discipline. Unlike maps, biological mechanism diagrams seem to fit in the idea of democratic practice of image-making in the first place because of their tight link with the research activity. This contrasts mechanism diagrams with maps. Below discusses two aspects of this.

Firstly, biological mechanism diagrams synthesise heterogeneous perspectives due to the collaborative and interactive nature of mechanism research. Such synthesis of heterogeneity is not to offer a totalising and absolute view for the mechanisms but to provide a space for interaction and integration amongst diverse perspectives. One can consider biological mechanism research as principally “harnessing collective intelligence” (O'Reilly, 2005, as cited in Gartner, 2009, 234). This is the way some cartographers have proposed to practice mapping in the era of Web 2.0. Cartographers have had painstaking discussions on the inevitability and benefits of having partial

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<sup>123</sup> Del Casino and Hanna, 2005.

perspectives embedded in maps<sup>124</sup>. But in biological mechanism diagrams, selected perspectives from different interests are configured together into the visual form by the researchers. Different from a traditional anxiety in cartography about providing the ultimate representations of the world, mechanism diagrams are made for highly practical purposes that must reflect local interests yet invite remote interactions. Map studies have come to a similar conclusion through debates around the inevitable locality and selectivity<sup>125</sup>. Without encountering much challenge like this, biological mechanism diagrams inherently serve to do what cartographers recently consider as the function of maps: “the map is both the spatial embodiment of knowledge and a stimulus for further cognitive engagement” (Cosgrove, 1999, 1).

Secondly, researchers engaged in mechanism research are co-developers of the explanatory models. Thus the distinction between the producer and the user of biological mechanism diagrams is relatively vague, compared with traditional practice of map-making. This may be largely due to the difference between the practices of making scientific images and maps. As argued above, biologists produce diagrams not only to communicate with the wider community but also to “communicate with themselves” at different stages of theory-developing. These two identities—producer and user—merge in the same individuals. In this sense, debates around authority and the production-consumption dichotomy are less sharper in the study of diagram-making than cartography<sup>126</sup>.

In the case of theory competition but not collaboration, there may be debates on the authority of specific models and their visual representations. Yet such debates are different from the cartographic concern about the authoritative status of maps. Instead, they are related to the competition over explanatory power of the models. This has to do with the philosophical discussion on mechanism themselves, which this study does not cover (as already clarified in Section 2.4). The cartographic concern focuses on the democratisation of mapping and map-making practices, problematising the binary between production and consumption<sup>127</sup>. Such a concern challenges the traditional hegemony of cartographer's expert knowledge. It interrogates the one-way dissemination of messages embedded in maps from cartographers to the map-user. The authority of maps is shaken not because it loses the explanatory power but because there cannot be static and ultimate representations of the world. In the case of biological mechanism research, I follow Chang's view (2005) and consider that the competition between different systems of practice is a way of interacting. The competition is thus as productive as collaboration. In this sense, the worries about any hegemony of single diagram-producer (and its underlying perspective) or one-way dissemination of messages appear to be irrelevant. The diagrams as the *media for interacting* do not lose their position. They are still made by the practitioners who are simultaneously the producer and the user, the encoder and the interpreter.

## 5.7 Conclusion

The key argument of this chapter is that mechanism diagrams synthesise heterogeneous components and emerge as supersigns with both asserting and engaging power. Such a synthesis of heterogeneity results from the intertwined relationship between the making of diagrams and the practice of biological mechanism research. Diagrams simultaneously embody the features of practice and are a part of practice.

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<sup>124</sup> See Kitchin, Perkins and Dodge, 2009; Proppen, 2009.

<sup>125</sup> Ibid.

<sup>126</sup> Authorities and social factors, however, are likely to dominate local practice of diagram-making. I am not arguing that diagram-making in biology is absolutely free of such debates. My point is that, since biological mechanism diagrams are the reflection of research practice, they also reflect the highly collaborative and interactive nature of it.

<sup>127</sup> For example, Del Casino and Hanna (2005) have nicely reviewed and made critical comparison between many important accounts that have contributed to related debates in the past two to three decades.

Section 5.1 to 5.4 discussed some features of different diagram types based on the results of survey. Section 5.1 argues that, with some exceptions, the themes of diagrams in apoptosis research have shown a shift of visual focus from the descriptive object type to the explanatory mechanism type. The exceptions can be explained by the qualitative results and also suggest a similar pattern of emphasis shift. Section 5.2, 5.3, and 5.4 show the intimate link between the growing complexity of biological perspectives and the evolution of diagrams. Section 5.2 counters an assumption that biological diagrams are about resemblances to entities. Section 5.3 explores different kinds of visual innovation. Modular use of visual elements implies the important role of visual consistency in biological arguments. Employment of non-specialist visual vocabulary contributes to both developing new visual language and visual reasoning. Plurality of the meanings of arrows reflects the relationship between the complexity of ideas and the reshaping of visual language. Mitochondria icons are special cases, which tend to be emphasised in apoptosis diagrams. This emphasis may result from their unique structure and their centrality in apoptotic mechanisms.

Section 5.5 and 5.6 focused on developing the key argument of this thesis, exploring how research practice is embodied by mechanism diagrams. Mechanism diagrams embed the interactive features and the pragmatic value of the culture of mechanism research. To contextualise these points in existing scholarship, the next chapter will end this thesis by discussing its most important contributions and recommending questions for future study.

## Chapter Six: Conclusion

This chapter centres on two themes. Section 6.1 presents the main contributions to the existing literature. Section 6.2 discusses potential future topics based on the framework established by this thesis.

### 6.1 Main arguments and contributions

This thesis argues that biological diagrams engage diverse perspectives in real-world intervention through synthesising heterogeneity. Engagement of heterogeneous perspectives invites dialogues between them, giving rise to novel ideas. In this thesis, three key features of biological diagrams—synthetic, heterogeneous, engaging—were concluded from a large scale of survey on the diagrams. These features make the diagrams simultaneously the representations of models and a part of the modelling practice.

By achieving the above argument, this thesis contributes to the existing literature in three aspects.

Firstly, this study is the first systematic survey of a large population of technical diagrams (plus the text adjacent to them) in contemporary biology. Its quantitative analysis has extracted the comprehensive patterns of visualisation in expert communication. The main finding is a shift of visual focus from description of entities to explanation of phenomena. This shift is demonstrated in the relative changes between the prevalence of object and mechanism diagrams, paralleling a shift of focus in biological practice from morphology to mechanistic modelling. Historians have observed that many biological disciplines have gone through such a shift during the twentieth century. This thesis took a novel approach via analysing the visual expression of knowledge and argues that cell biology exhibited this trend, too.

Secondly, this study is also the first qualitative analysis of a large population of biological diagrams. It did not concentrate on special and elegant cases but has investigated a large population (see Table 3.1 for scale). It shows that the increasing reliance on mechanism diagrams paralleled the growth of complexity of the contents. Such a growth refers to not only an increase of iconographic resources but also an enrichment of perspectives. Importantly, not only the density of component perspectives grows but also their relationships multiply. This is why the contents become more complex. Different perspectives represent different local interests and methodologies, while approaching the same phenomena. This thesis analysed the embedding of localities in visual contents and concluded that mechanism diagrams visually integrate diverse perspectives.

Thirdly, this thesis argues that diagrams are increasingly *useful* in the development of mechanism research due to their synthetic capability. Because they integrate heterogeneous perspectives, they serve as the media for interaction within the expert community. Such interactions provoke productive dialogues between remote local practices, leading to the generation of novel meanings. Therefore, mechanism diagrams are powerful in two ways. They are powerful in asserting ideas because of the novelty emerging from their synthesis of heterogeneity. They are also powerful in engaging the researchers in physically controlling the mechanisms. This comes from their mediating role between the practices of knowing and intervening in the mechanisms. The qualitative results from analysing the complexity of mechanism diagrams explain the quantitative pattern of their prevalence. Namely, diagrams are increasingly used by the practitioners because their role in constructing cell models is crucial in two ways: epistemic and communicative. I have shown that these two functions are inseparable from each other.

## 6.2 Suggestions for future study

The above conclusions have created hypotheses for future study. A central question is: assuming that diagrams in biological mechanism research are vehicles for integration of, and interaction between, heterogeneous perspectives, we want to know *how they work*. That is, how the making of diagrams plays epistemological and communicative roles in the practice.

This study has proved that diagrams are a part of biological reasoning and conceptualisation, so we want to study the activity of the making of mechanism diagrams. This should involve probing the process of translating and transforming data, ideas and knowledge to iconographic resources. Such a future study can include the decision-making process on selection and creation of the components: (1) visual elements, compositions, and styles; (2) ideas and perspectives. In the case of making diagrams through collaboration between scientists and artists, one should pay attention to the dialogue between the two disciplines. This thesis has also argued that mechanism diagrams are the media for communicating different local perspectives and different stages of model development, but its phenomenologist approach focused only on the media content (ie. images themselves). Future study should examine the consumption of media content, exploring the factors of effective visual communication and conceptualisation. I tentatively suggest the following methods for studying the above questions: ethnographic and sociological methods<sup>128</sup>, as well as content and audience analysing methods in media communications.

This thesis has established a methodological framework for comprehensively analysing large populations of images. This framework should be employed by future study on *how diagrams work* in terms of extending the surveys to areas other than apoptosis. This will not only test the framework of this thesis but also reflect, in a broader sense, on the interplay between visual culture and contemporary biological practice. I also recommend comparative studies between biology and other sciences in terms of the relationship between visualisation, reasoning, and communication. Following or paralleling such comparative studies, the role of diagrams in communicating biology to the public can be examined. This direction is based upon the notion of engaging power of diagrams argued by this study. These topics may provide insights in the functions of new biological visuals.

Both the methodological and the theoretical frameworks created by this thesis should be applied to other areas of specialisation. This thesis maintains that biological diagrams engage the user because of their epistemic and communicative roles. Such roles result from their capability of *synthesising heterogeneity*. I envision that the main arguments of this thesis will shed light on the synthetic and heterogeneous features of diagrams in a broader context: the new era of visual culture. This is an era when visuals increasingly gain engaging power not only in biosciences but also across a range of social arenas.

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<sup>128</sup> For a similar approach, recent examples are McLeod and Nersessian (2014) and Burnston et al. (2015).



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**Synthesising Heterogeneity:  
trends of visibility in biological sciences circa 1970s - 2000s**

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Submitted for the degree of Doctor of Philosophy  
in Science and Technology Studies  
Two volumes in total

**Volume II**

## **Volume II: Figures**

Figures of this thesis are presented in this volume in numerical sequence.

Text and tables are presented in Volume I.

This volume does not contain any argument and is intended to be viewed adjacent to correlated sections in Volume I.

The numbering of figures follows this format: “chapter.section.(subsection.)number”, eg. Figure 4.2.1.1 means the first figure of Section 4.2.1 in Chapter Four.

**Figure 2.1**

Diagram of blood circulation through the heart. From Bechtel, William. *Discovering Cell Mechanisms: The Creation of Modern Cell Biology*. Cambridge: Cambridge University Press, 2006., Figure 2.2, p.31.

### **Figure 2.2**

Diagram of the citric acid cycle, demonstrating that abstract ideas are transformed and translated to visual forms of representation. From Lodish, Harvey, Arnold Berk, S Lawrence Zipursky, Paul Matsudaira, David Baltimore, and James Darnell. *Molecular Cell Biology*. 4 ed. New York: W. H. Freeman, 2000, Figure 16-12.

### **Figure 2.3**

Example diagram of biological mechanism (1). From Taylor, R. C., C. Adrain, and S. J. Martin. "Proteases, Proteasomes and Apoptosis: Breaking Ub Is Hard to Do." *Cell Death Differ* 12, no. 9 (2005): 1213-17, Figure 1.

**Figure 2.4**

Example diagram of biological mechanism (2). From Lodish, et al., *Molecular Cell Biology*. 4 ed. New York: W. H. Freeman, 2000, Figure 20-49.



### **Figure 2.5**

Example visual product of simultaneous image-manipulation and nature-simulation. From Karin, Michael, Tom Huxford, Alexander Hoffmann, and Gourisankar Ghosh. "Understanding the Logic of I $\kappa$ B:NF- $\kappa$ B Regulation in Structural Terms." In *NF- $\kappa$ B in Health and Disease*, edited by Michael Karin, 1-24. Berlin: Springer, 2011, Figure 5.

**Figure 2.6**

Lynch's photo-diagram pair. From Lynch, Michael. "The Externalized Retina: Selection and Mathematization in the Visual Documentation of Objects in the Life Sciences." In *Representation in Scientific Practice*, edited by Michael Lynch and Steve Woolgar. London: The MIT Press, 1990, p.159, Figure 2.

**Figure 2.7**

Example diagram of modelling through reassembly of an object in the photograph.  
From: Ibid., p.166, Figure 5.

**Figure 2.8**

Added rational descriptions in diagrams. Lynch uses these examples to demonstrate the notion of mathematization. From: Ibid., p.173, Figure 8.

**A**



**B**

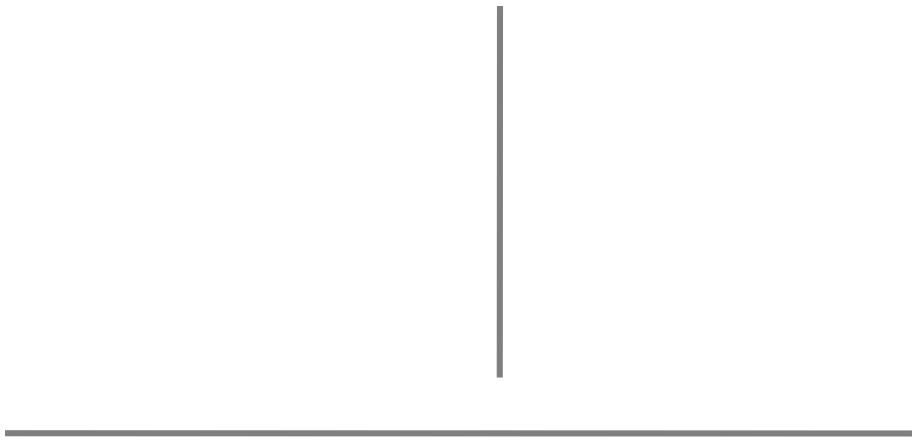
**Figure 3.1**

Example object diagrams. A: from Devireddy, Laxminarayana R., Claude Gazin, et al. "A Cell-Surface Receptor for Lipocalin 24p3 Selectively Mediates Apoptosis and Iron Uptake." *Cell* 123, no. 7 (2005): 1293-305, Figure 1A; B: from Shaham, Shai, and H. Robert Horvitz. "An Alternatively Spliced C. Elegans Ced-4 Rna Encodes a Novel Cell Death Inhibitor." *Cell* 86, no. 2 (1996): 201-08, Figure 1B.



### **Figure 3.2**

Example object diagrams. Upper: from Limoli, Charles L., Mark I. Kaplan, et al. "Chromosomal Instability and Its Relationship to Other End Points of Genomic Instability." *Cancer Research* 57, no. 24 (1997): 5557-63, Figure 7a, b; lower: from Mundle, Suneel D., and Gurveen Saberwal. "Evolving Intricacies and Implications of E2f1 Regulation." *The FASEB Journal* 17, no. 6 (2003): 569-74, Figure 1.



### Figure 3.3

Example object diagrams. Upper left: from Trusolino, Livio, Luisa Pugliese, et al. "Interactions between Scatter Factors and Their Receptors: Hints for Therapeutic Applications." *The FASEB Journal* 12, no. 13 (1998): 1267-80, Figure 1; upper right: from Zhou, Zheng, Erika Hartwig, et al. "Ced-1 Is a Transmembrane Receptor That Mediates Cell Corpse Engulfment in *C. Elegans*." *Cell* 104, no. 1 (2001): 43-56, Figure 3d, e, f. Lower: from Debnath, Jayanta, Kenna R. Mills, et al. "The Role of Apoptosis in Creating and Maintaining Luminal Space within Normal and Oncogene-Expressing Mammary Acini." *Cell* 111, no. 1 (2002): 29-40, Figure 6A.



### Figure 3.4

Example chemical structure diagrams. Upper: from Zhou, James H., Balakrishna S. Pai, et al. "Discovery of Short, 3'-Cholesterol-Modified DNA Duplexes with Unique Antitumor Cell Activity." *Cancer Research* 54, no. 22 (1994): 5783-87, Figure 2; middle: from Neuzil, Jirí, Tobias Weber, et al. "Induction of Cancer Cell Apoptosis by  $\alpha$ -Tocopheryl Succinate: Molecular Pathways and Structural Requirements." *The FASEB Journal* 15, no. 2 (2001): 403-15, Scheme 1; lower: from Clackson, Tim, Wu Yang, et al. "Redesigning an Fkbp-Ligand Interface to Generate Chemical Dimerizers with Novel Specificity." *PNAS* 95, no. 18 (1998): 10437-42, Figure 1.





### Figure 3.5

Example experimental design diagrams. Upper: from Socolovsky, Merav, Amy E. J. Fallon, et al. "Fetal Anemia and Apoptosis of Red Cell Progenitors in Stat5a / 5b / Mice: A Direct Role for Stat5 in Bcl-Xl Induction." *Cell* 98, no. 2 (1999): 181-91, Figure 2A;

Lower: from Krieser, RJ, KS MacLea, et al. "Deoxyribonuclease Iialpha Is Required During the Phagocytic Phase of Apoptosis and Its Loss Causes Perinatal Lethality." *Cell Death and Differentiation* 9, no. 9 (2002): 956-62, Figure 1A.

### **Figure 3.6**

Example experimental design diagram. From Limoli, Charles L., Mark I. Kaplan, et al. "Chromosomal Instability and Its Relationship to Other End Points of Genomic Instability." *Cancer Research* 57, no. 24 (1997): 5557-63, Figure 1.

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### **Figure 3.7**

Example mechanism diagrams. Upper: from Jiang, Zhe, and Eldad Zacksenhaus. "Activation of Retinoblastoma Protein in Mammary Gland Leads to Ductal Growth Suppression, Precocious Differentiation, and Adenocarcinoma." *The Journal of Cell Biology* 156, no. 1 (2002): 185-98, Figure 9A, B; lower: from Vaux, David L, and Stanley J Korsmeyer. "Cell Death in Development." *Cell* 96, no. 2 (1999): 245-54, Figure 1.



### Figure 3.8

Example mechanism diagrams. Left: from Ravi, Rajani, Gauri C. Bedi, et al. "Regulation of Death Receptor Expression and Trail/Apo2l-Induced Apoptosis by Nf-[Kappa]B." *Nat Cell Biol* 3, no. 4 (2001): 409-16, Figure 6;  
Right: from Salvesen, Guy S., and Vishva M. Dixit. "Caspase Activation: The Induced-Proximity Model." *PNAS* 96, no. 20 (1999): 10964-67, Figure 1.



### Figure 3.9

Example mechanism diagrams. Upper: from Lin, Kuo- I., Joseph A. DiDonato, et al. "Suppression of Steady-State, but Not Stimulus-Induced Nf- $\kappa$ B Activity Inhibits Alphavirus-Induced Apoptosis." *The Journal of Cell Biology* 141, no. 7 (1998): 1479-87, Figure 7; lower: from Rathmell, Jeffrey C., and Craig B. Thompson. "Pathways of Apoptosis in Lymphocyte Development, Homeostasis, and Disease." *Cell* 109, no. 2 (2002): S97-S107, Figure 2.

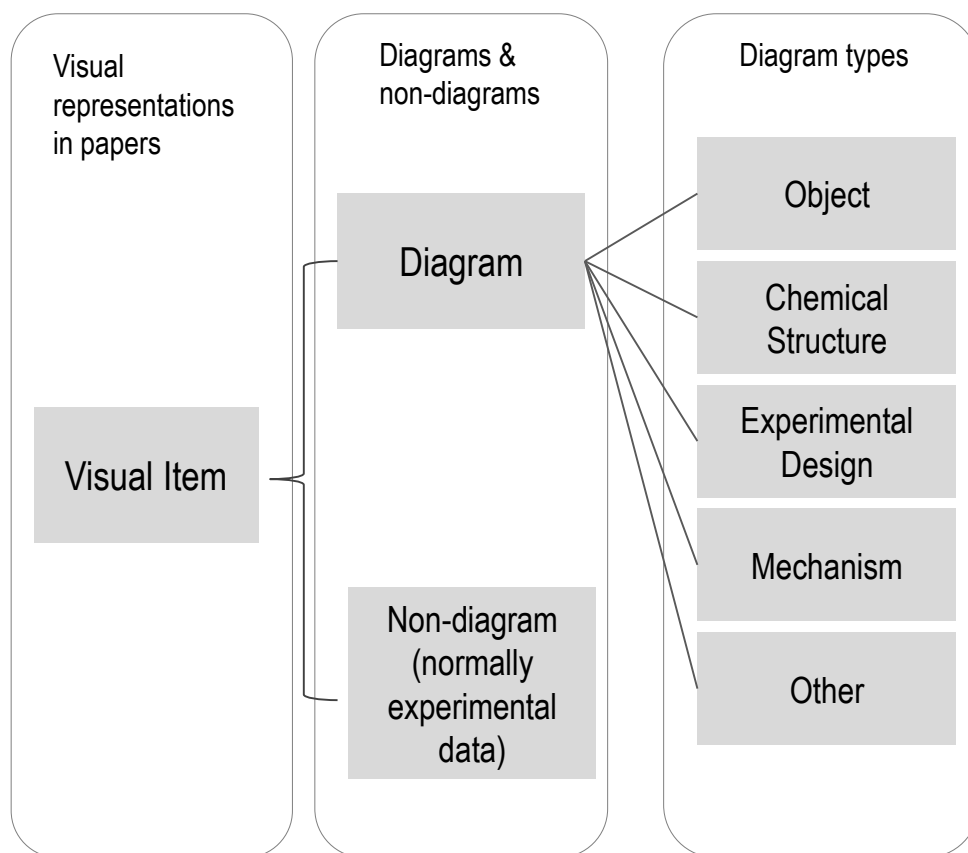
**Figure 3.10**

Example mechanism diagram. From Gill, Catherine, Ruben Mestral, et al. "Losing Heart: The Role of Apoptosis in Heart Disease—a Novel Therapeutic Target?" *The FASEB Journal* 16, no. 2 (2002): 135-46, Figure 1.



**Figure 3.11**

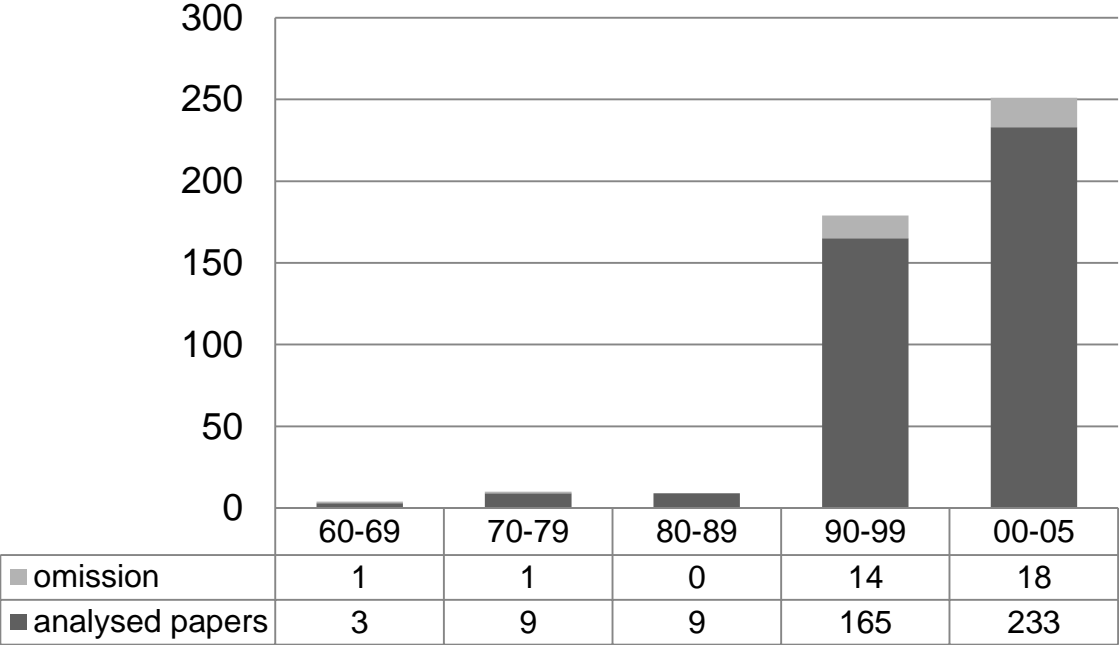
Example “other” diagrams. Left: from Ellis, Hilary M., and H. Robert Horvitz. "Genetic Control of Programmed Cell Death in the Nematode *C. Elegans*." *Cell* 44, no. 6 (1986): 817-29, Figure 8; Right: from Marko, Nicholas F., Paul B. Dieffenbach, et al. "Does Metabolic Radiolabeling Stimulate the Stress Response? Gene Expression Profiling Reveals Differential Cellular Responses to Internal Beta Vs. External Gamma Radiation." *The FASEB Journal* 17, no. 11 (2003): 1470-86, Figure 7.



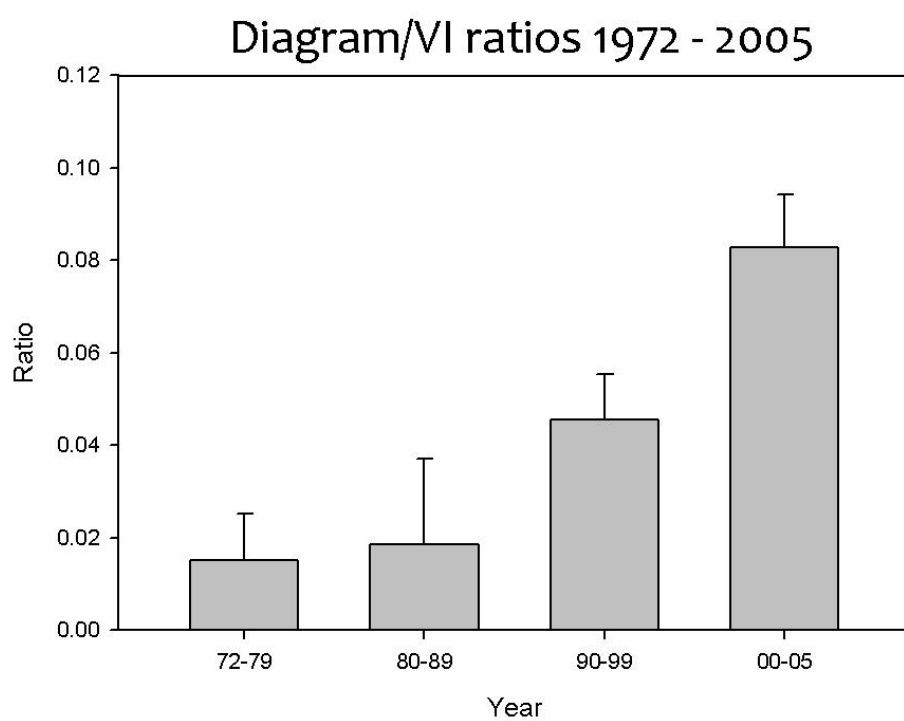
**Figure 3.12**

The structure of taxonomy used in this thesis.



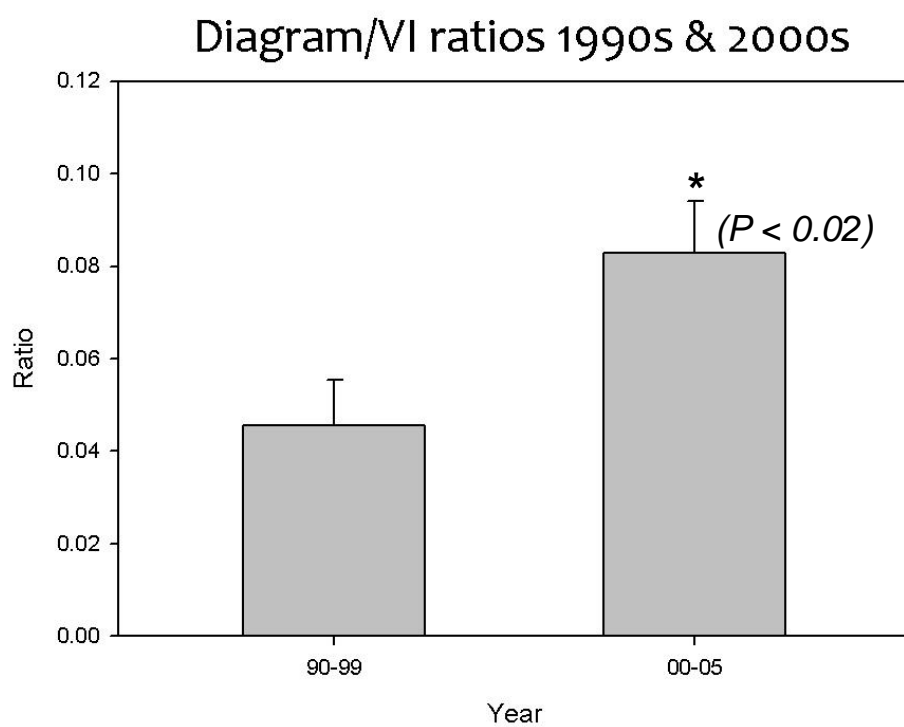


**Figure 4.2.1.1**  
Data profile of *JCB*: search results and analysed papers.



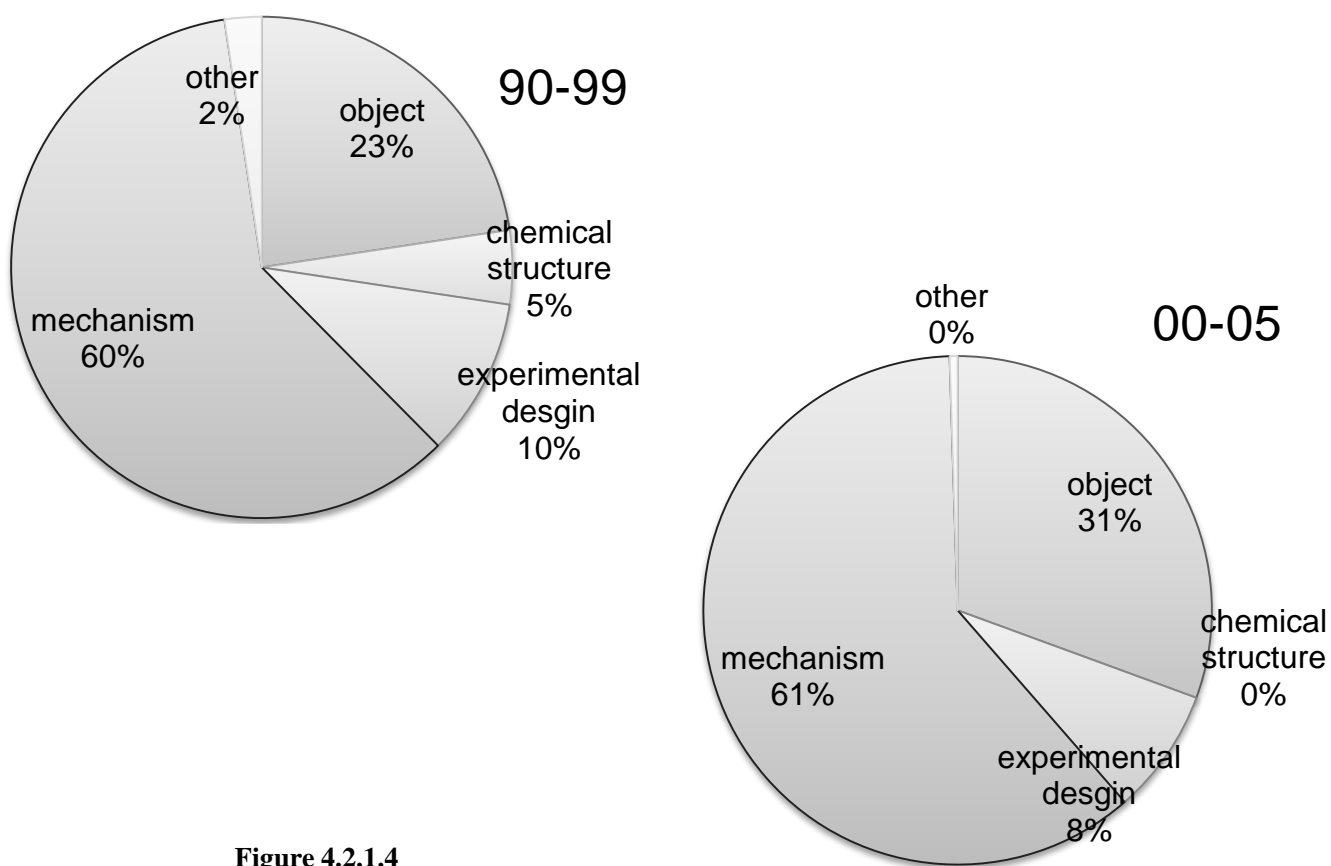
**Figure 4.2.1.2**

D/VIs in *JCB*, 1972–2005.



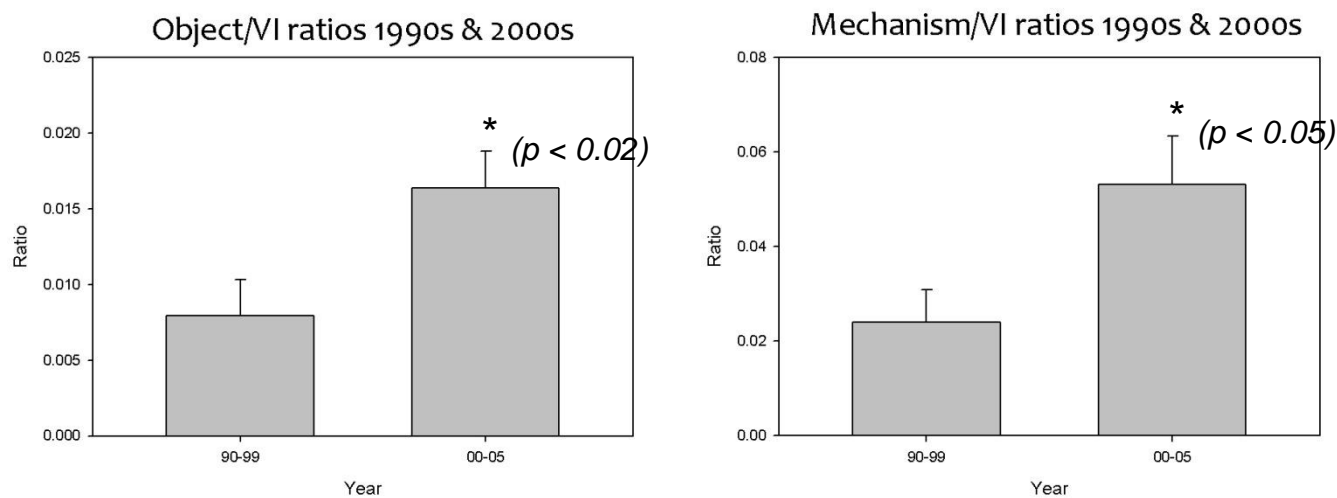
**Figure 4.2.1.3**

D/VIs in *JCB*, 1990s and 2000s.



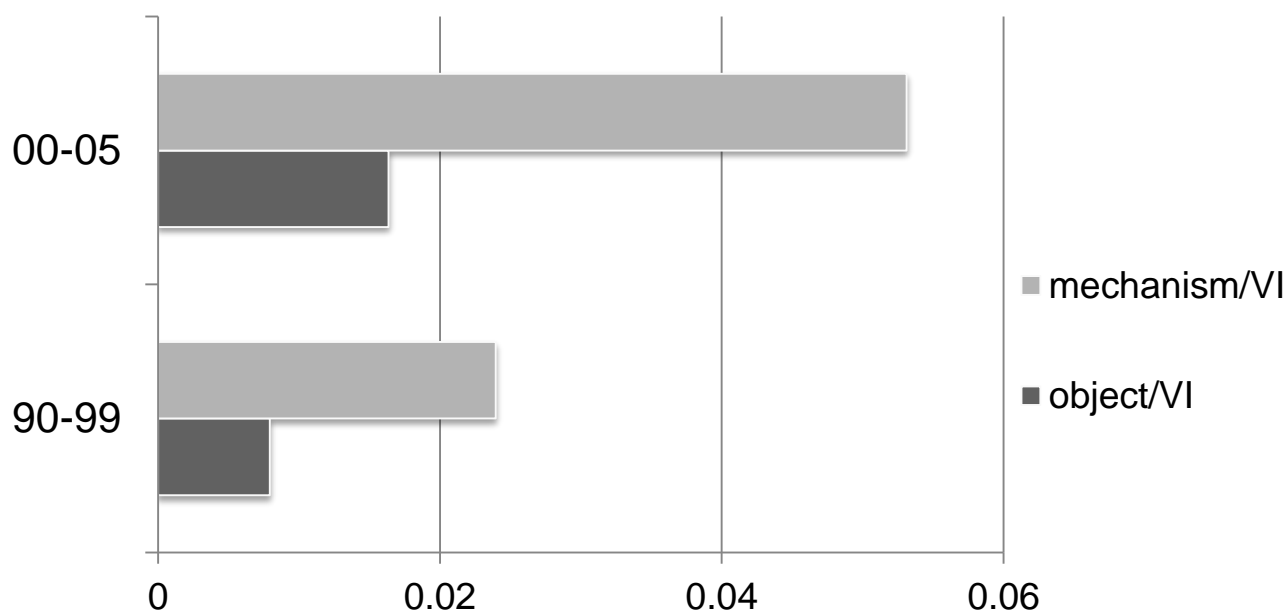
**Figure 4.2.1.4**

Proportions of five diagram types in *JCB*, 1990s and 2000s.



**Figure 4.2.1.5**

D/VIs of two major diagram types (object and mechanism) in *JCB*, 1990s and 2000s.



**Figure 4.2.1.6**

Comparison of D/VIs between object and mechanism types in the 1990s and the 2000s. In both decades the differences are statistically significant. Their difference in the 2000s is even larger.

**Figure 4.2.1.7**

Object type. From Pilar, G., and L. Landmesser. "Ultrastructural Differences During Embryonic Cell Death in Normal and Peripherally Deprived Ciliary Ganglia." *The Journal of Cell Biology* 68, no. 2 (1976): 339-56, Figure 18.

**Figure 4.2.1.8**

Object type. From Hermiston, M. L., and J. I. Gordon. "In Vivo Analysis of Cadherin Function in the Mouse Intestinal Epithelium: Essential Roles in Adhesion, Maintenance of Differentiation, and Regulation of Programmed Cell Death." *The Journal of Cell Biology* 129, no. 2 (1995): 489-506, Figure 1.



**Figure 4.2.1.9**

Object type. From Shimizu, Shigeomi, Yosuke Matsuoka, et al. "Essential Role of Voltage-Dependent Anion Channel in Various Forms of Apoptosis in Mammalian Cells." *The Journal of Cell Biology* 152, no. 2 (2001): 237-50, Figure 1A.

**Figure 4.2.1.10**

Object type. From Alexander, C M, E W Howard, et al. "Rescue of Mammary Epithelial Cell Apoptosis and Entactin Degradation by a Tissue Inhibitor of Metalloproteinases-1 Transgene." *The Journal of Cell Biology* 135, no. 6 (1996): 1669-77, Figure 7b.

**Figure 4.2.1.11**

Object type. From von Ahsen, Oliver, Christian Renken, et al. "Preservation of Mitochondrial Structure and Function after Bid- or Bax-Mediated Cytochrome C Release." *The Journal of Cell Biology* 150, no. 5 (2000): 1027-36, Figure 4.

**Figure 4.2.1.12**

Experimental design type. From Janda, Elzbieta, Kerstin Lehmann, et al. "Ras and Tgf $\beta$  Cooperatively Regulate Epithelial Cell Plasticity and Metastasis: Dissection of Ras Signaling Pathways." *The Journal of Cell Biology* 156, no. 2 (2002): 299-314, left: Figure 7A, right: Figure 8A.

**Figure 4.2.1.13**

“Other” type. From Deckwerth, T. L., and E. M. Johnson. "Temporal Analysis of Events Associated with Programmed Cell Death (Apoptosis) of Sympathetic Neurons Deprived of Nerve Growth Factor." *The Journal of Cell Biology* 123, no. 5 (1993): 1207-22, Figure 12.

**Figure 4.2.1.14**

“Other” type. From Estus, S., W. J. Zaks, et al. "Altered Gene Expression in Neurons During Programmed Cell Death: Identification of C-Jun as Necessary for Neuronal Apoptosis." *The Journal of Cell Biology* 127, no. 6 (1994): 1717-27, Figure 5.

**Figure 4.2.1.15**

Mechanism type. From Cardarelli, P. M., I. N. Crispe, et al. "Preferential Expression of Fibronectin Receptors on Immature Thymocytes." *The Journal of Cell Biology* 106, no. 6 (1988): 2183-90, Figure 6.

**A**

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**B**

**Figure 4.2.1.16**

Mechanism type. A: from Li, W C, J R Kuszak, et al. "Lens Epithelial Cell Apoptosis Appears to Be a Common Cellular Basis for Non-Congenital Cataract Development in Humans and Animals." *The Journal of Cell Biology* 130, no. 1 (1995): 169-81, Figure 10;

B: from Toyoshima, Fumiko, Tetsuo Moriguchi, et al. "Fas Induces Cytoplasmic Apoptotic Responses and Activation of the Mkk7-Jnk/Sapk and Mkk6-P38 Pathways Independent of Cpp32-Like Proteases." *The Journal of Cell Biology* 139, no. 4 (1997): 1005-15, Figure 8.



**Figure 4.2.1.17**

Mechanism type. From Deshmukh, M, J Vasilakos, et al. "Genetic and Metabolic Status of Ngf-Deprived Sympathetic Neurons Saved by an Inhibitor of Ice Family Proteases." *The Journal of Cell Biology* 135, no. 5 (1996): 1341-54, Figure 10.

**Figure 4.2.1.18**

Mechanism type. From Nechushtan, Amotz, Carolyn L. Smith, et al. "Bax and Bak Coalesce into Novel Mitochondria-Associated Clusters During Apoptosis." *The Journal of Cell Biology* 153, no. 6 (2001): 1265-76, Figure 8.

**Figure 4.2.1.19**

Mechanism type. From Bossenmeyer-Pourié, Carine, Rama Kannan, et al. "The Trefoil Factor 1 Participates in Gastrointestinal Cell Differentiation by Delaying G1-S Phase Transition and Reducing Apoptosis." *The Journal of Cell Biology* 157, no. 5 (2002): 761-70, Figure 8.

**Figure 4.2.1.20**

Mechanism type. From Pardo, Julián, Alberto Bosque, et al. "Apoptotic Pathways Are Selectively Activated by Granzyme a and/or Granzyme B in Ctl-Mediated Target Cell Lysis." *The Journal of Cell Biology* 167, no. 3 (2004): 457-68, Figure 7.

**Figure 4.2.1.21**

Mechanism type. From Jones, Peter Lloyd, Julie Crack, et al. "Regulation of Tenascin-C, a Vascular Smooth Muscle Cell Survival Factor That Interacts with the  $\alpha_v\beta_3$  Integrin to Promote Epidermal Growth Factor Receptor Phosphorylation and Growth." *The Journal of Cell Biology* 139, no. 1 (1997): 279-93, Figure 9.

**Figure 4.2.1.22**

Mechanism type. From Li, Shaohua, David Harrison, et al. "Matrix Assembly, Regulation, and Survival Functions of Laminin and Its Receptors in Embryonic Stem Cell Differentiation." *The Journal of Cell Biology* 157, no. 7 (2002): 1279-90, Figure 10.

#### **Figure 4.2.1.23**

Mechanism type. From Lane, Jon D., Mailys A.S. Vergnolle, et al. "Apoptotic Cleavage of Cytoplasmic Dynein Intermediate Chain and P150gluedstops Dynein-Dependent Membrane Motility." *The Journal of Cell Biology* 153, no. 7 (2001): 1415-26, Figure 10. The numbering (A, B) is from the original paper.

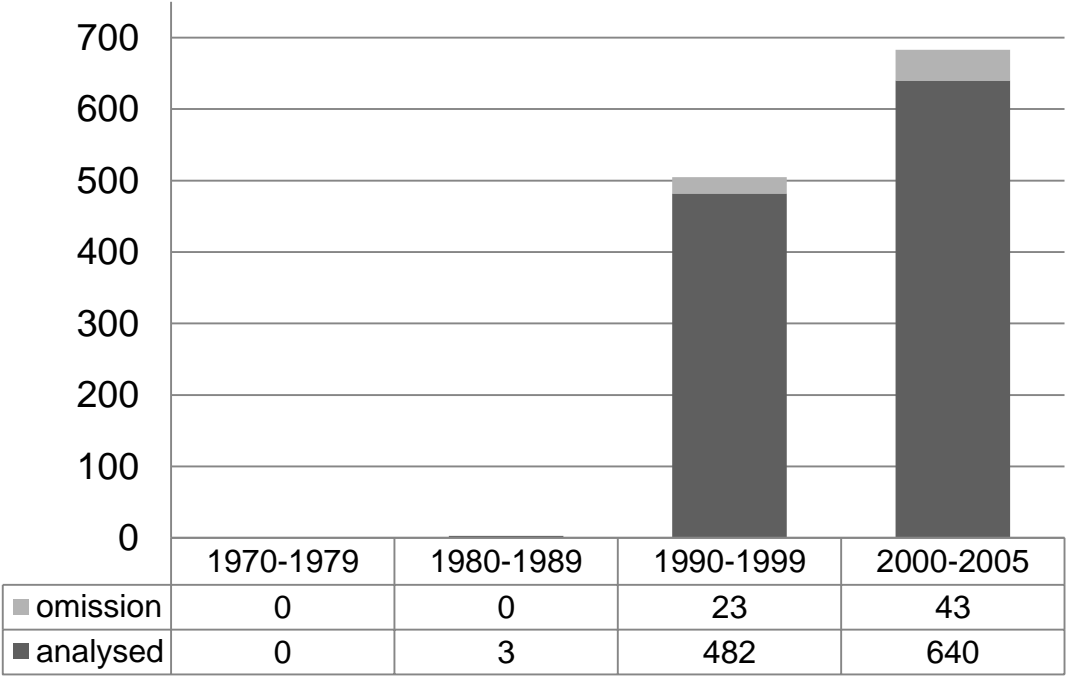
**Figure 4.2.1.24**

Mechanism type. From Screaton, Robert A., Linda Z. Penn, et al. "Carcinoembryonic Antigen, a Human Tumor Marker, Cooperates with Myc and Bcl-2 in Cellular Transformation." *The Journal of Cell Biology* 137, no. 4 (1997): 939-52, Figure 10.



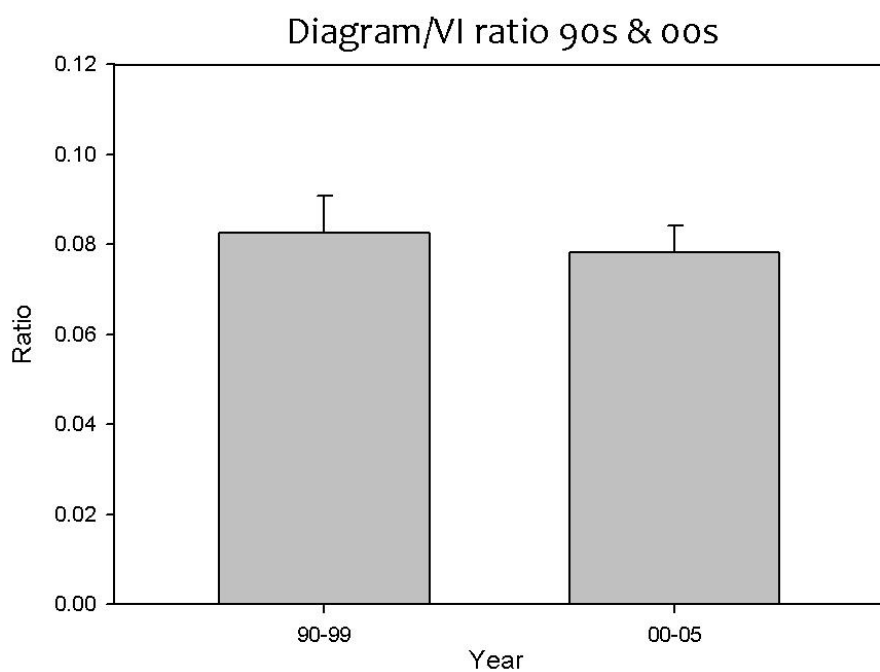
**Figure 4.2.1.25**

Mechanism type. From Bentele, M., I. Lavrik, et al. "Mathematical Modeling Reveals Threshold Mechanism in Cd95-Induced Apoptosis." *The Journal of Cell Biology* 166, no. 6 (2004): 839-51, Figure 1.

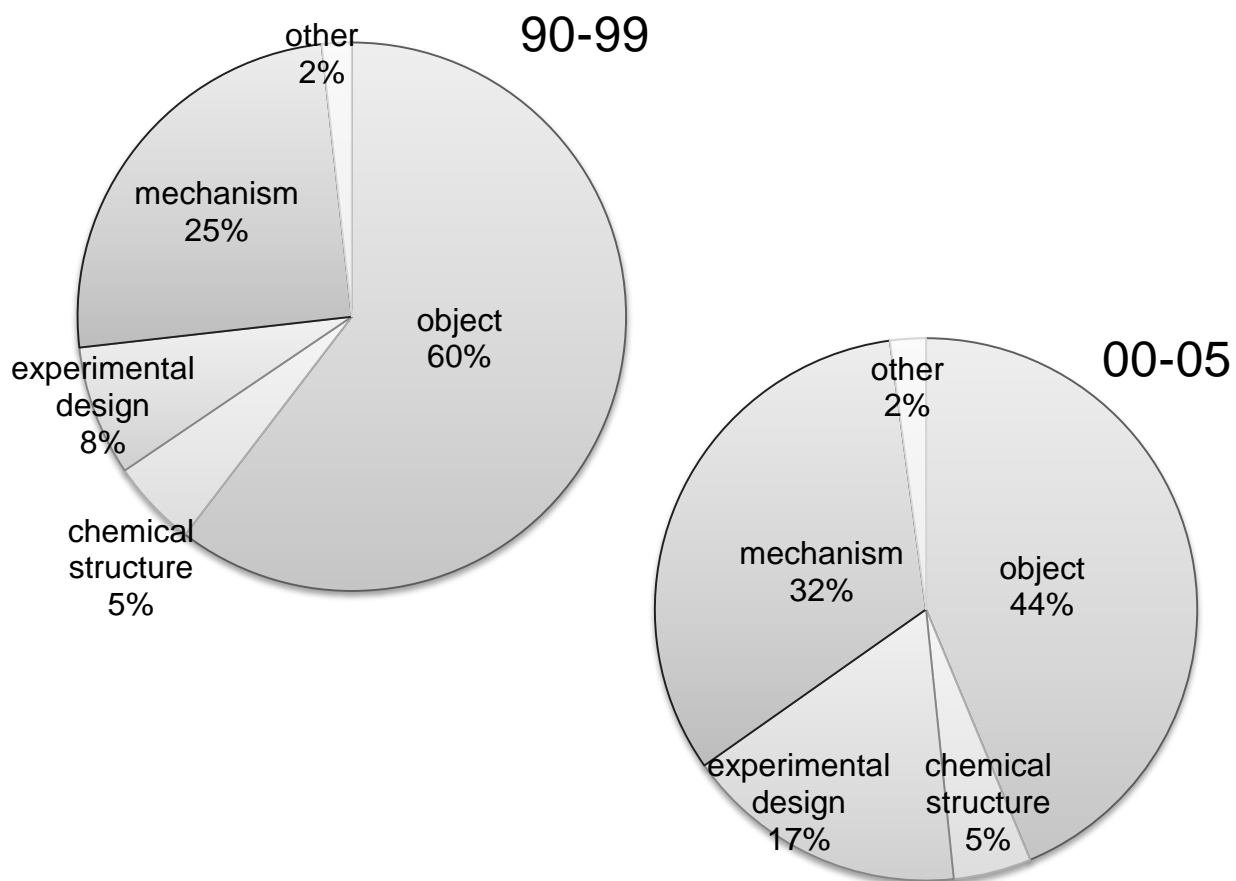


**Figure 4.2.2.1**

Data profile of *PNAS*: search results and analysed papers.



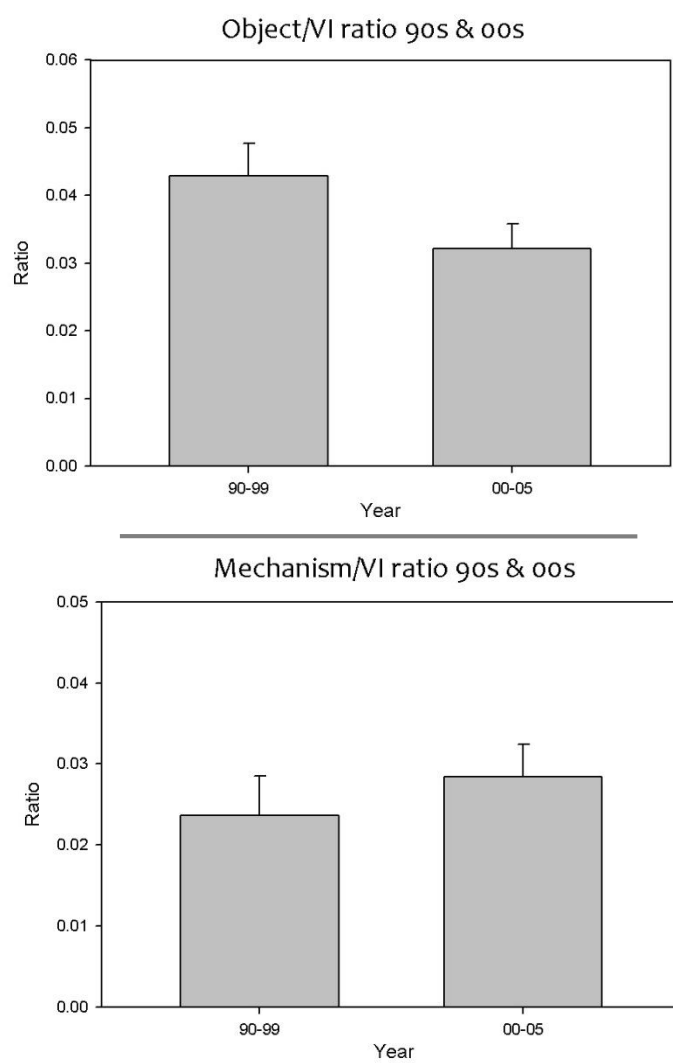
**Figure 4.2.2.2**  
D/VIs in *PNAS*, 1990–2005.



**Figure 4.2.2.3**

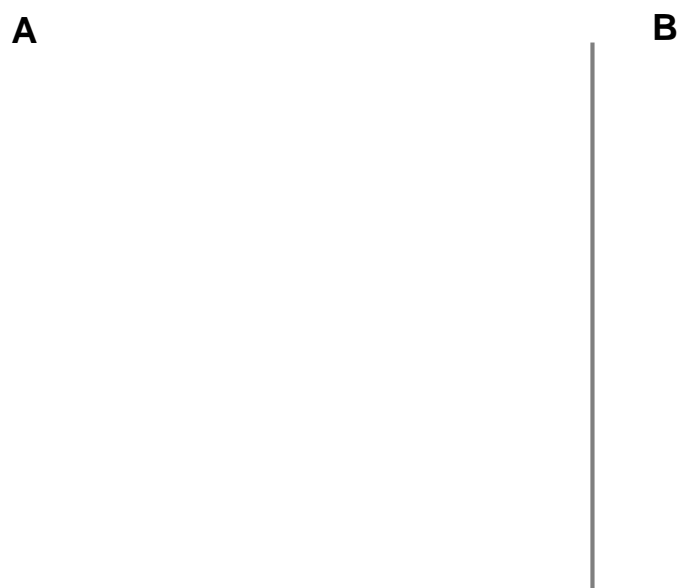
Distributions of all five diagram types in *PNAS*, 1990–2005.

**Figure 4.2.2.4**  
D/VIs of two prevalent types of diagrams in *PNAS*, 1990–2005.



**Figure 4.2.2.5**

Object type. From Piacenza, LucÃa, Gonzalo Peluffo, et al. "L-Arginine-Dependent Suppression of Apoptosis in Trypanosoma Cruzi: Contribution of the Nitric Oxide and Polyamine Pathways." *PNAS* 98, no. 13 (2001): 7301-06, Figure 1.



**Figure 4.2.2.6**

Object type. A: from Zhu, Yanan, Bradley J. Swanson, et al. "Constitutive Association of the Proapoptotic Protein Bim with Bcl-2-Related Proteins on Mitochondria in T Cells." *PNAS* 101, no. 20 (2004): 7681-86, Figure 3A; B: from Ashur-Fabian, Osnat, Aaron Avivi, et al. "Evolution of P53 in Hypoxia-Stressed Spalax Mimics Human Tumor Mutation." *PNAS* 101, no. 33 (2004): 12236-41, Figure 4B.

**Figure 4.2.2.7**

Object type. From Kim, Sanguk, Aaron K. Chamberlain, et al. "Membrane Channel Structure of *Helicobacter Pylori* Vacuolating Toxin: Role of Multiple Gxxxg Motifs in Cylindrical Channels." *PNAS* 101, no. 16 (2004): 5988-91, Figure 4.



**Figure 4.2.2.8**

Object type. From Belyakov, Oleg V., Stephen A. Mitchell, et al. "Biological Effects in Unirradiated Human Tissue Induced by Radiation Damage up to 1 Mm Away." *Proceedings of the National Academy of Sciences of the United States of America* 102, no. 40 (2005): 14203-08, Figure 1.

**A**

**B**

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**Figure 4.2.2.9**

Experimental design type. A: from Chen, Ching-Kang, Marie E. Burns, et al. "Abnormal Photoresponses and Light-Induced Apoptosis in Rods Lacking Rhodopsin Kinase." *PNAS* 96, no. 7 (1999): 3718-22, Figure 1A: B: from Sarkar, Devanand, Zao-zhong Su, et al. "Dual Cancer-Specific Targeting Strategy Cures Primary and Distant Breast Carcinomas in Nude Mice." *PNAS* 102, no. 39 (2005): 14034-39, Figure 1.

**Figure 4.2.2.10**

Experimental design type. From Xia, Chunzhi, Wenbin Ma, et al. "Regulation of the P21-Activated Kinase (Pak) by a Human G $\beta$ -Like Wd-Repeat Protein, Hpip1." *PNAS* 98, no. 11 (2001): 6174-79, Figure 3A.

**Figure 4.2.2.11**

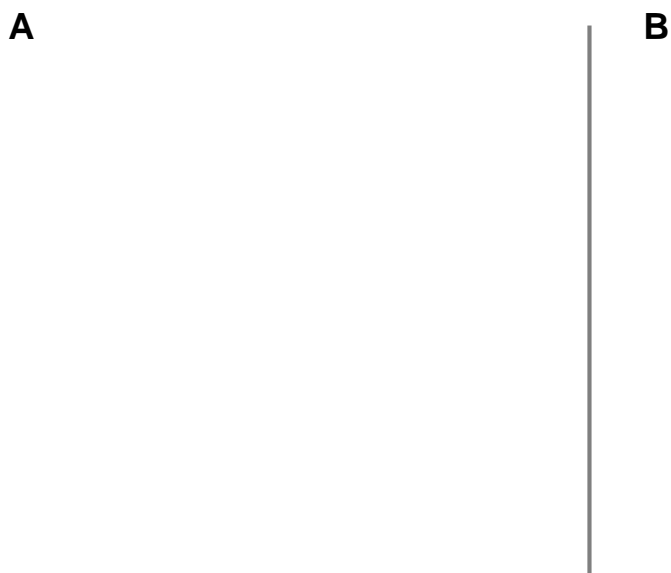
Experimental design type. From Vila, Miquel, Vernice Jackson-Lewis, et al. "Bax Ablation Prevents Dopaminergic Neurodegeneration in the 1-Methyl- 4-Phenyl-1,2,3,6-Tetrahydropyridine Mouse Model of Parkinson's Disease." *PNAS* 98, no. 5 (2001): 2837-42, Figure 2A.

**Figure 4.2.2.12**

“Other” type. From Aulak, Kulwant S., Masaru Miyagi, et al. "Proteomic Method Identifies Proteins Nitrated in Vivo During Inflammatory Challenge." *PNAS* 98, no. 21 (2001): 12056-61, Figure 5.

**Figure 4.2.2.13**

“Other” type. From Juric, Dejan, Sanja Sale, et al. "Gene Expression Profiling Differentiates Germ Cell Tumors from Other Cancers and Defines Subtype-Specific Signatures." *PNAS* 102, no. 49 (2005): 17763-68, Figure 3.



**Figure 4.2.2.14**

Mechanism type. A: from Linette, G. P., Y. Li, et al. "Cross Talk between Cell Death and Cell Cycle Progression: Bcl-2 Regulates Nfat-Mediated Activation." *PNAS* 93, no. 18 (1996): 9545-52, Figure 9; B: from Mayer, M., and M. Noble. "N-Acetyl-L-Cysteine Is a Pluripotent Protector against Cell Death and Enhancer of Trophic Factor-Mediated Cell Survival in Vitro." *PNAS* 91, no. 16 (1994): 7496-500, Figure 5.

**A**

**B**



**Figure 4.2.2.15**

Mechanism type. A: from Xiang, Jialing, Debra. T Chao, et al. "Bax-Induced Cell Death May Not Require Interleukin 1 $\beta$ -Converting Enzyme-Like Proteases." *PNAS* 93, no. 25 (1996): 14559-63, Figure 5;  
B: from Sedlak, T. W., Z. N. Oltvai, et al. "Multiple Bcl-2 Family Members Demonstrate Selective Dimerizations with Bax." *PNAS* 92, no. 17 (1995): 7834-38, Figure 6.



**Figure 4.2.2.16**

Mechanism type. From Vaux, D. L., and A. Strasser. "The Molecular Biology of Apoptosis." *PNAS* 93, no. 6 (1996): 2239-44, Figure 1.

**Figure 4.2.2.17**

Mechanism type. From Healy, Zachary R., Norman H. Lee, et al. "Divergent Responses of Chondrocytes and Endothelial Cells to Shear Stress: Cross-Talk among Cox-2, the Phase 2 Response, and Apoptosis." *PNAS* 102, no. 39 (2005): 14010-15, Figure 8.

**Figure 4.2.2.18**

Mechanism type. From Perier, Celine, Kim Tieu, et al. "Complex I Deficiency Primes Bax-Dependent Neuronal Apoptosis through Mitochondrial Oxidative Damage." *PNAS* 102, no. 52 (2005): 19126-31, Figure 5.

**Figure 4.2.2.19**

Mechanism type. From Lee, Cheol-Koo, David B. Allison, et al. "Transcriptional Profiles Associated with Aging and Middle Age-Onset Caloric Restriction in Mouse Hearts." *PNAS* 99, no. 23 (2002): 14988-93, Figure 3.

**Figure 4.2.2.20**

Mechanism type. From Shen, Zhi-Xiang, Zhan-Zhong Shi, et al. "All-Trans Retinoic Acid/As<sub>2</sub>O<sub>3</sub> Combination Yields a High Quality Remission and Survival in Newly Diagnosed Acute Promyelocytic Leukemia." *PNAS* 101, no. 15 (2004): 5328-35, Figure 3.

**A**

**B**

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**Figure 4.2.2.21**

Mechanism type. A: from Van Stry, Melanie, Andrius Kazlauskas, et al. "Distinct Effectors of Platelet-Derived Growth Factor Receptor- $\alpha$  Signaling Are Required for Cell Survival During Embryogenesis." *PNAS* 102, no. 23 (2005): 8233-38, Figure 1C; B: from Shu, Hong-Bing, Masahiro Takeuchi, et al. "The Tumor Necrosis Factor Receptor 2 Signal Transducers Traf2 and C-Iap1 Are Components of the Tumor Necrosis Factor Receptor 1 Signaling Complex." *PNAS* 93, no. 24 (1996): 13973-78, Figure 6.

**Figure 4.2.2.22**

Mechanism type. From Lillig, Christopher Horst, Carsten Berndt, et al. "Characterization of Human Glutaredoxin 2 as Iron-Sulfur Protein: A Possible Role as Redox Sensor." *PNAS* 102, no. 23 (2005): 8168-73, Figure 6.

**A**

**B**

**C**

**Figure 4.2.2.23**

A: experimental design type; B, C: mechanism type. A: from Tse, Eric, and Terence H. Rabbitts. "Intracellular Antibody-Caspase-Mediated Cell Killing: An Approach for Application in Cancer Therapy." *PNAS* 97, no. 22 (2000): 12266-71, Figure 1A; B: from Fig. 2A; C: from Fig. 4A.



**A**

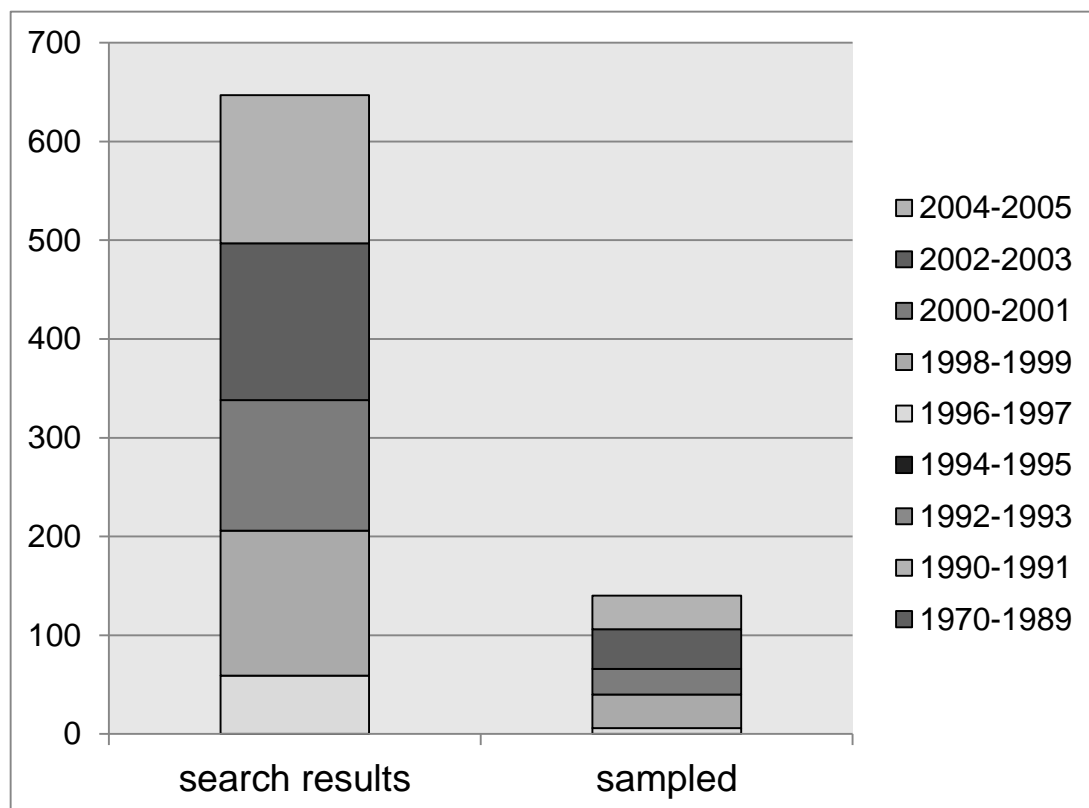
**B**

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**Figure 4.2.2.24**

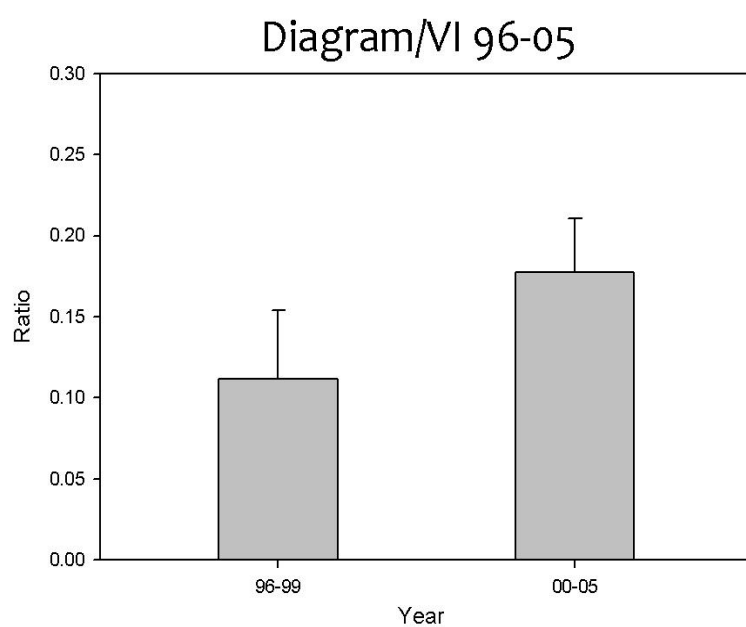
Mechanism type. A: from Suzuki, Erika, Kazuko Handa, et al. "Sphingosine-Dependent Apoptosis: A Unified Concept Based on Multiple Mechanisms Operating in Concert." *PNAS* 101, no. 41 (2004): 14788-93, Figure 4;

B: from Lodish, Harvey, Arnold Berk, et al. *Molecular Cell Biology*. 5th ed. New York: W. H. Freeman, 2003, Figure 22-32.

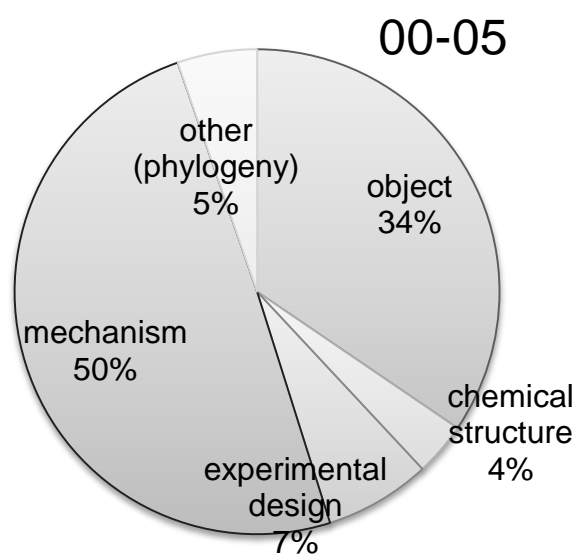
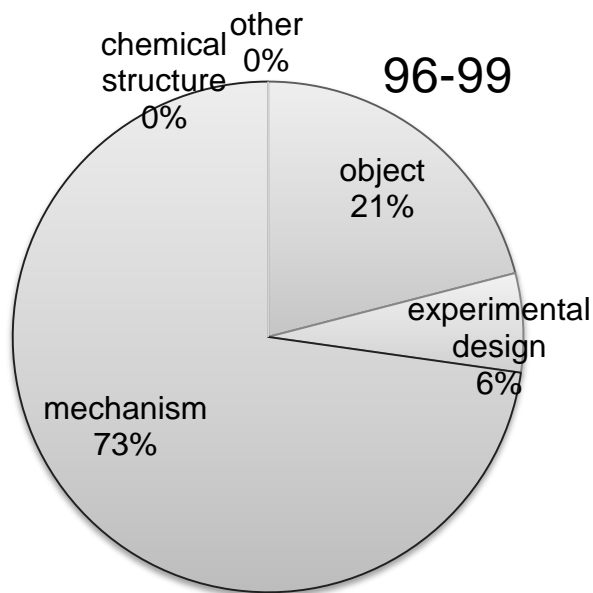


**Figure 4.2.3.1**

Data profile of *Cell Death and Differentiation*.

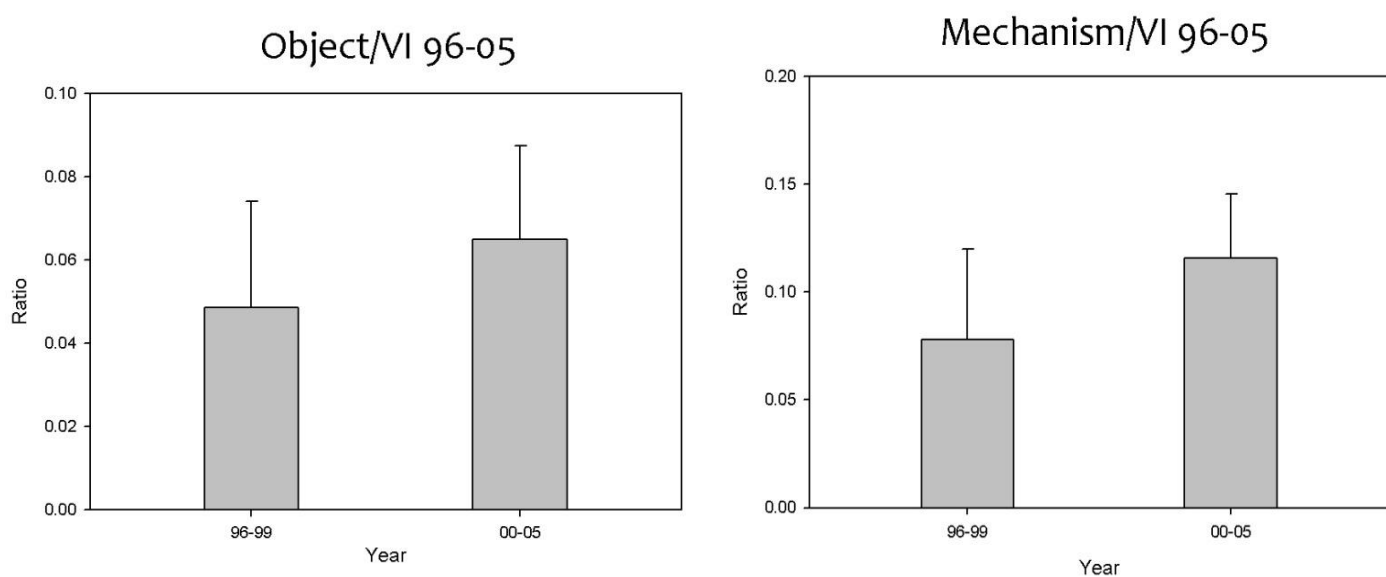


**Figure 4.2.3.2**  
*D/VIs in Cell Death Differ, 1996–2005.*



**Figure 4.2.3.3**

Proportion of diagram types in *Cell Death Differ*, 1996–2005.



**Figure 4.2.3.4**

D/VIs of two prevalent diagram types in *Cell Death Differ*, 1996–2005.

### **Figure 4.2.3.5**

Object type. From Wolfe, E Lu and J. "Lysosomal Enzymes in the Macronucleus of Tetrahymena During Its Apoptosis-Like Degradation." *Cell Death and Differentiation* 8, no. 3 (2001), 289, Figure 1.

### **Figure 4.2.3.6**

Object type. From Ferrando-May, E. "Nucleocytoplasmic Transport in Apoptosis." *Cell Death Differ* 12, no. 10 (2005): 1263-76, Figure 1.

### **Figure 4.2.3.7**

Experimental design type. From Donnay, Serge Pampfer and Isabelle. "Apoptosis at the Time of Embryo Implantation Inmouse and Rat." *Cell Death and Differentiation* 6 (1999): 533, Figure 1B.



### **Figure 4.2.3.8**

Experimental design type. From L A O'Reilly, P Ekert, N Harvey, V Marsden, L Cullen, D L Vaux, G Hacker, C Magnusson, M Pakusch, F Cecconi, K Kuida, A Strasser, D C S Huang and S Kumar. "Caspase-2 Is Not Required for Thymocyte or Neuronal Apoptosis Even Though Cleavage of Caspase-2 Is Dependent on Both Apaf-1 and Caspase-9." *Cell Death and Differentiation* 9 (2002): 832, Figure 2.

### **Figure 4.2.3.9**

Experimental design type. From Evelyne SeÂgal-Bendirdjian, Lionel Mannone1 and Alain Jacquemin-Sablon. "Alteration in P53 Pathway and Defect in Apoptosis Contribute Independently to Cisplatin-Resistance." *Cell Death and Differentiation* 5 (1998): 390, Figure 7.

**A**

**B**

**Figure 4.2.3.10**

Chemical structure type. A: from Zuco, V., C. Zanchi, G. Cassinelli, C. Lanzi, R. Supino, C. Pisano, R. Zanier, V. Giordano, E. Garattini, and F. Zunino. "Induction of Apoptosis and Stress Response in Ovarian Carcinoma Cell Lines Treated with St1926, an Atypical Retinoid." *Cell Death Differ* 11, no. 3 (2003): 280-89, Figure 1; B: from Malet, G., A. G. Martin, M. Orzaez, M. J. Vicent, I. Masip, G. Sanclimens, A. Ferrer-Montiel, I. Mingarro, A. Messeguer, H. O. Fearnhead, and E. Perez-Paya. "Small Molecule Inhibitors of Apaf-1-Related Caspase-3/-9 Activation That Control Mitochondrial-Dependent Apoptosis." *Cell Death Differ* 13, no. 9 (2005): 1523-32, Figure 1a.

### **Figure 4.2.3.11**

Mechanism type. From E A Slee, S A Keogh and S J Martin. "Cleavage of Bid During Cytotoxic Drug and Uv Radiation-Induced Apoptosis Occurs Downstream of the Point of Bcl-2 Action and Is Catalysed by Caspase-3: A Potential Feedback Loop for Amplification of Apoptosis-Associated Mitochondrial Cytochrome C Release." *Cell Death and Differentiation* 7 (2000): 556, Figure 7.

### **Figure 4.2.3.12**

Mechanism type. From McDonnell, M. A., D. Wang, S. M. Khan, M. G. Vander Heiden, and A. Kelekar. "Caspase-9 Is Activated in a Cytochrome C-Independent Manner Early During Tnf[Alpha]-Induced Apoptosis in Murine Cells." *Cell Death Differ* 10, no. 9 (2003): 1005-15, Figure 9.

### **Figure 4.2.3.13**

Mechanism type. From Taylor, R. C., C. Adrain, and S. J. Martin. "Proteases, Proteasomes and Apoptosis: Breaking Ub Is Hard to Do." *Cell Death Differ* 12, no. 9 (2005): 1213-17, Figure 1.

### **Figure 4.2.3.14**

Mechanism type. From Bogler, O., and M. Weller. "International Hermelin Brain Tumor Center Symposium on Apoptosis." *Cell Death Differ* 10, no. 9 (2003): 1112-15, Figure1.

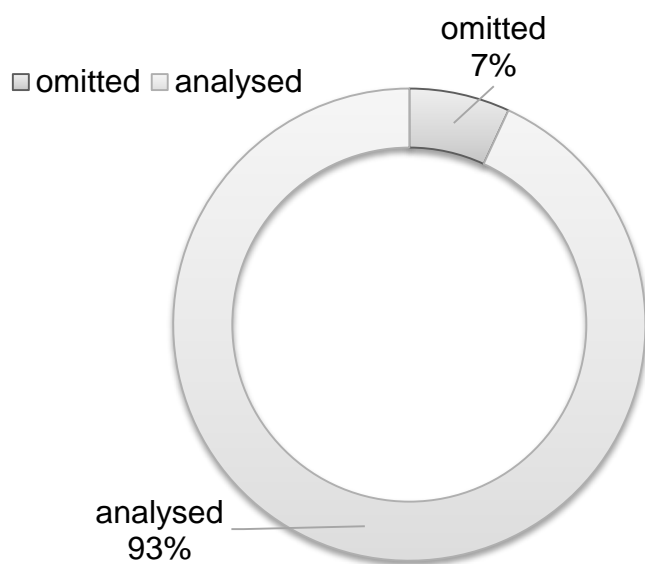
### **Figure 4.2.3.15**

“Other” type. From Aravind, E V Koonin and L. "Origin and Evolution of Eukaryotic Apoptosis: The Bacterial Connection." *Cell Death and Differentiation* 9 (2002): 394, Figure 1B.

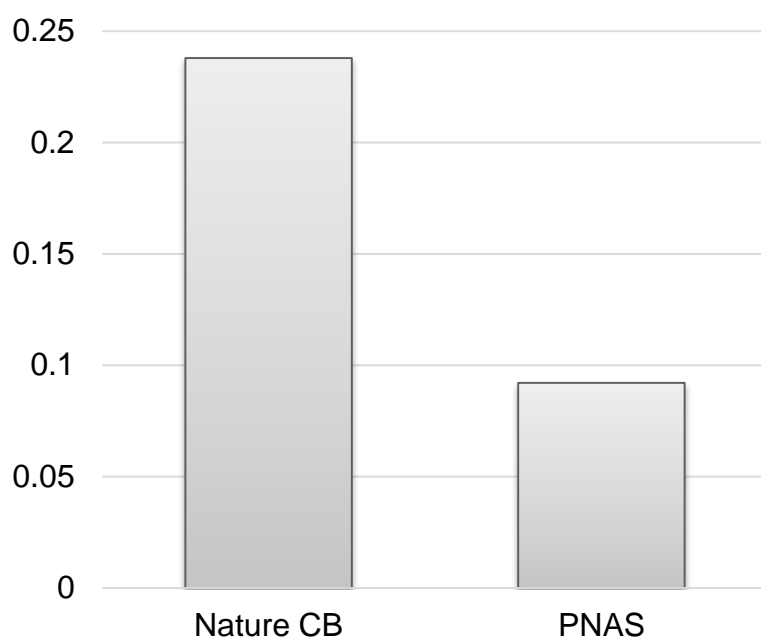


### **Figure 4.2.3.16**

“Other” type. From Doctor, K. S., J. C. Reed, A. Godzik, and P. E. Bourne. "The Apoptosis Database." *Cell Death Differ* 10, no. 6 (2003): 621-33, Figure 3.

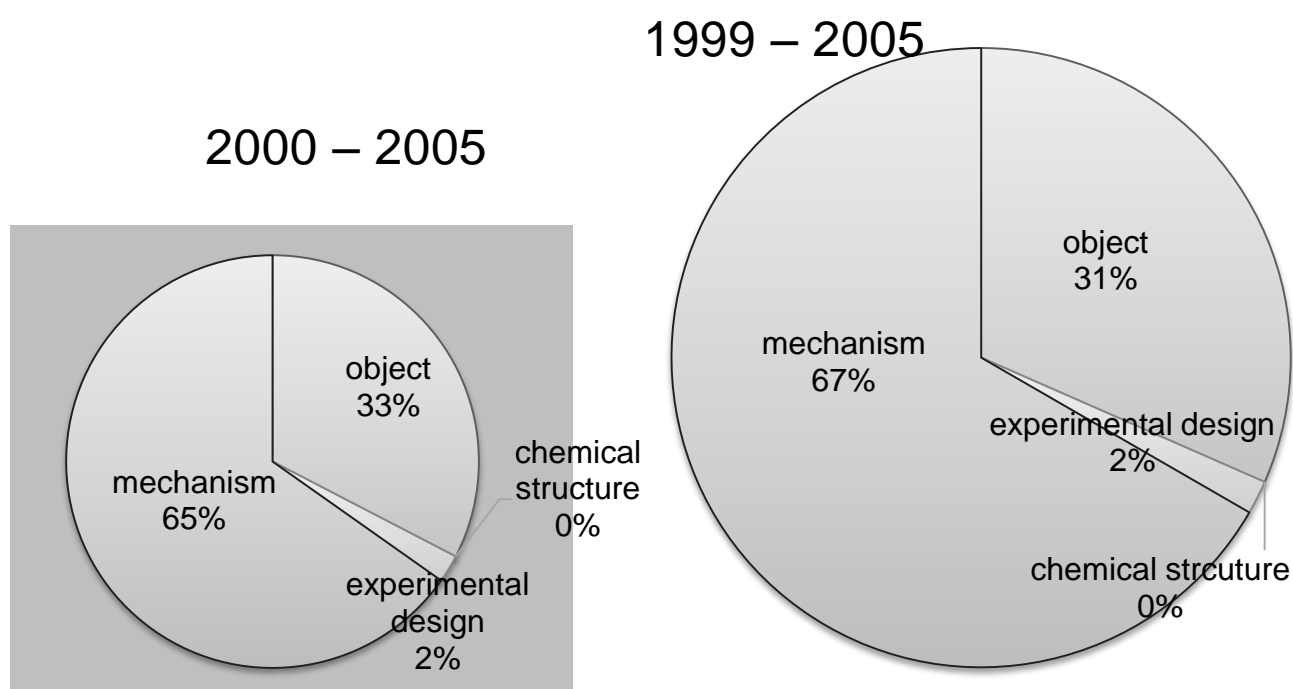


**Figure 4.2.4.1**  
Data profile of *Nature Cell Biology*.



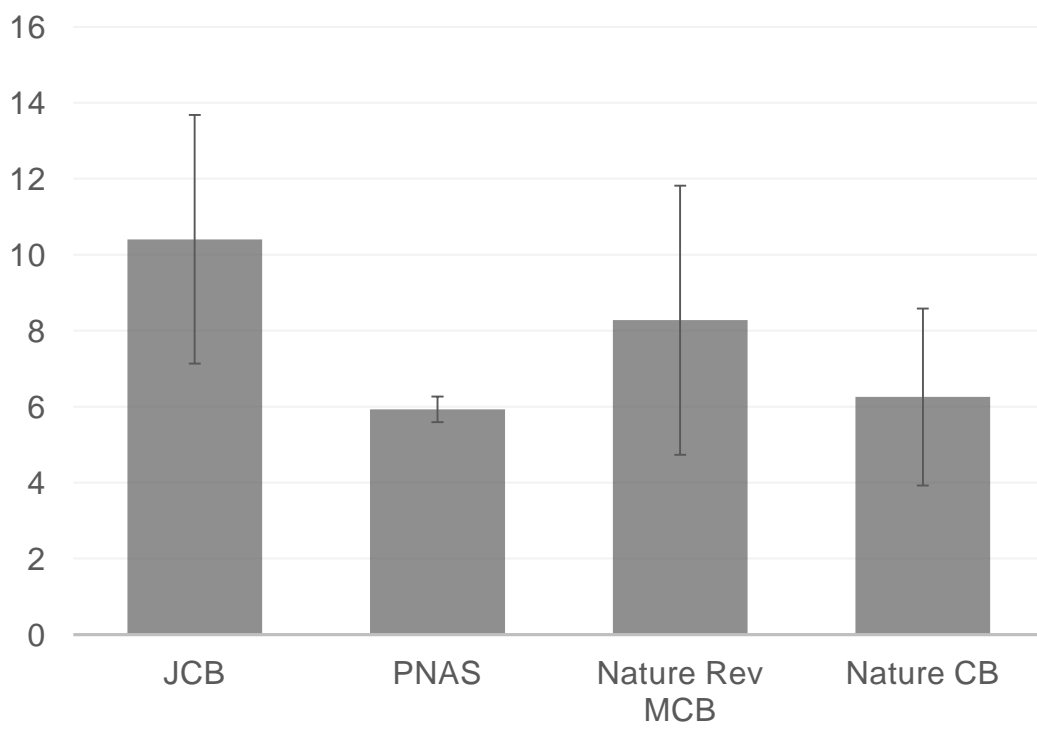
**Figure 4.2.4.2**

Comparison of D/VIs in *Nature Cell Biology* and *PNAS*.



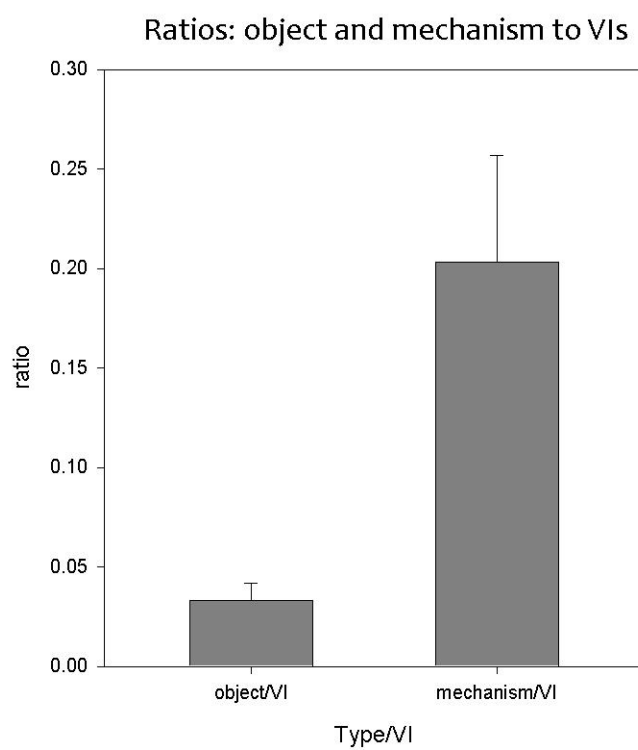
**Figure 4.2.4.3**

Proportions of diagram types in *Nature Cell Biology*. Right: whole period studied; left: 2000–2005.



**Figure 4.2.4.4**

Comparison of average paper sizes (as page numbers) between journals.



**Figure 4.2.4.5**

D/VIs in *Nature Cell Biology*, 1999–2005.

#### **Figure 4.2.4.6**

Object type. From Larisch, Sarit, Youngsuk Yi, Rona Lotan, Hedviga Kerner, Sarah Eimerl, W. Tony Parks, Yossi Gottfried, Stephanie Birkey Reffey, Mark P. de Caestecker, David Danielpour, Naomi Book-Melamed, Rina Timberg, Colin S. Duckett, Robert J. Lechleider, Hermann Steller, Joseph Orly, Seong-Jin Kim, and Anita B. Roberts. "A Novel Mitochondrial Septin-Like Protein, Arts, Mediates Apoptosis Dependent on Its P-Loop Motif." *Nat Cell Biol* 2, no. 12 (2000): 915-21, Figure 1a, b.

**Figure 4.2.4.7**

Object type. From Tanikawa, Chizu, Koichi Matsuda, Seisuke Fukuda, Yusuke Nakamura, and Hirofumi Arakawa. "P53rdl1 Regulates P53-Dependent Apoptosis." *Nat Cell Biol* 5, no. 3 (2003): 216-23, Figure 1b.



**A**

**B**

**Figure 4.2.4.8**

Mechanism type. A: from Yang, Shutong, Christin Kuo, John E. Bisi, and Myung K. Kim. "Pml-Dependent Apoptosis after DNA Damage Is Regulated by the Checkpoint Kinase Hcds1/Chk2." *Nat Cell Biol* 4, no. 11 (2002): 865-70, Figure 5d;

B: from Conery, Andrew R., Yanna Cao, E. Aubrey Thompson, Courtney M. Townsend, Tien C. Ko, and Kunxin Luo. "Akt Interacts Directly with Smad3 to Regulate the Sensitivity to Tgf-[Beta]-Induced Apoptosis." *Nat Cell Biol* 6, no. 4 (2004): 366-72, Figure 4e.

**A**

**B**

**Figure 4.2.4.9**

Mechanism type. A: from Vander Heiden, Matthew G., and Craig B. Thompson. "Bcl-2 Proteins: Regulators of Apoptosis or of Mitochondrial Homeostasis?" *Nat Cell Biol* 1, no. 8 (1999): E209-E16, Figure 4;

B: from Mattson, Mark P., and Sic L. Chan. "Calcium Orchestrates Apoptosis." *Nat Cell Biol* 5, no. 12 (2003): 1041-43, Figure 1.

**Figure 4.2.4.10**

Mechanism type. From Benhar, Moran, and Jonathan S. Stamler. "A Central Role for S-Nitrosylation in Apoptosis." *Nat Cell Biol* 7, no. 7 (2005): 645-46, Figure 1.

**Figure 4.2.4.11**

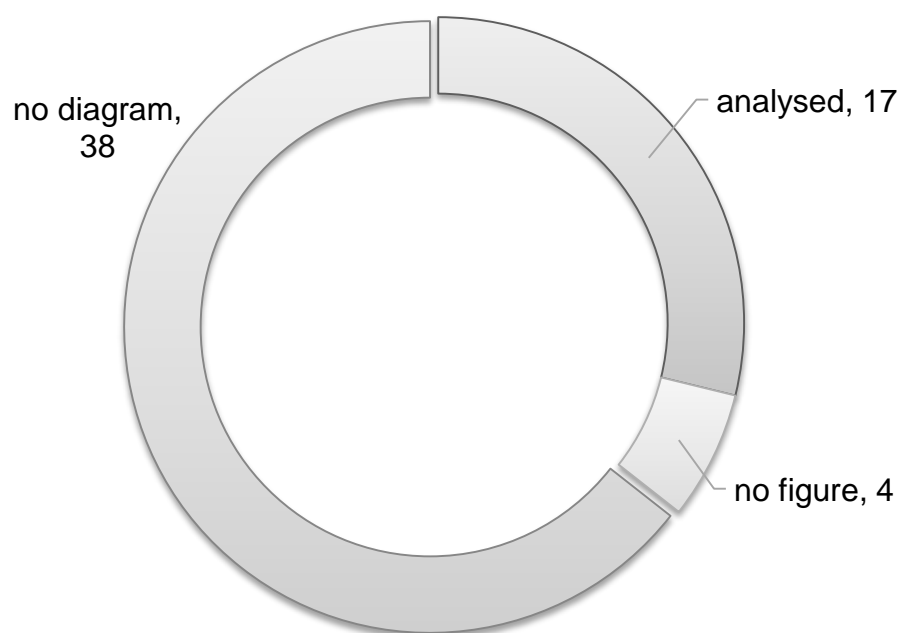
Mechanism type. From Palaga, Tanapat, and Barbara Osborne. "The 3d's of Apoptosis: Death, Degradation and Diaps." *Nat Cell Biol* 4, no. 6 (2002): E149-E51, Figure 1.

**Figure 4.2.4.12**

Mechanism type. From Hotchkiss, Richard S., Craig M. Coopersmith, Jonathan E. McDunn, and Thomas A. Ferguson. "The Sepsis Seesaw: Tilting toward Immunosuppression." *Nat Med* 15, no. 5 (2009): 496-97, Figure 1.

**Figure 4.2.4.13**

Mechanism type. From Scanga, Charles A., and JoAnne L. Flynn. "Mycobacterial Infections and the Inflammatory Seesaw." *Cell host & microbe* 7, no. 3 (2010): 177-79, Figure 1.



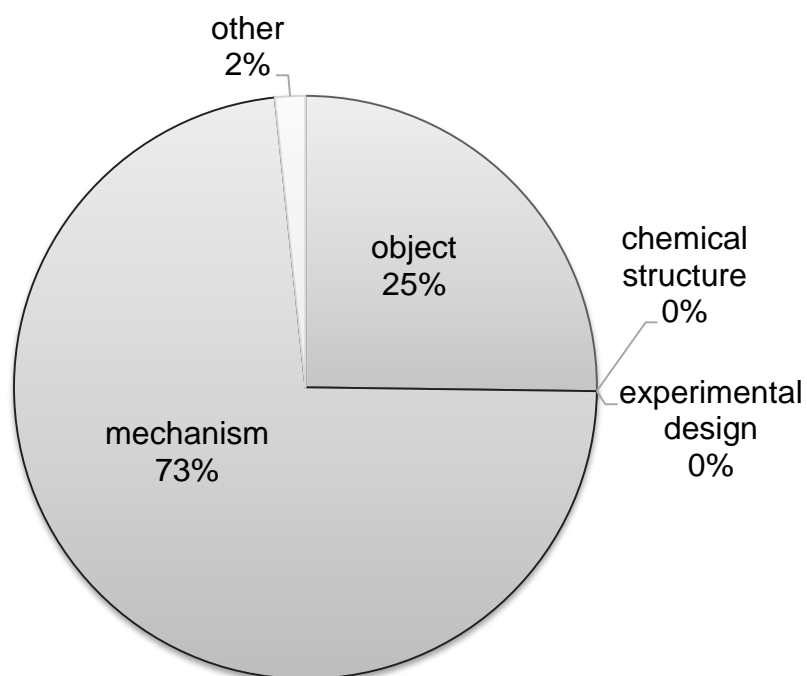
**Figure 4.2.5.1**

Data profile of *Nature Reviews Molecular Cell Biology*.

**Figure 4.2.5.2**

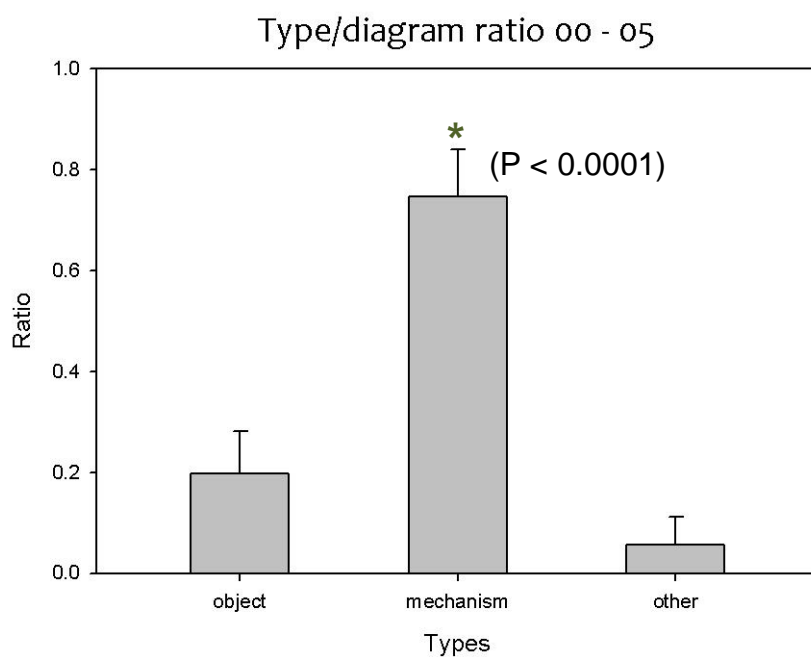
An example of figure from the “no diagram” category: metaphorical use of photograph. From "Molecular Assembly Line." *Nat Rev Mol Cell Biol* 2, no. 11 (2001): 790.





**Figure 4.2.5.3**

Proportions of diagram types in *Nat Rev Mol Cell Biol.*



**Figure 4.2.5.4**

D/VIs of three diagram types in *Nat Rev Mol Cell Biol.*

A

B

**Figure 4.2.5.5**

A: from Mitchell, Alison. "Bax to Bak." *Nat Rev Mol Cell Biol* 2, no. 1 (2001): 6, Figure 1;

B: from Riedl, Stefan J., and Yigong Shi. "Molecular Mechanisms of Caspase Regulation During Apoptosis." *Nat Rev Mol Cell Biol* 5, no. 11 (2004): 897, Figure 6.

A

B

**Figure 4.2.5.6**

A: from Riedl, Stefan J., and Yigong Shi (2004), Figure 1;

B: Salvesen, Guy S., and Colin S. Duckett. "Iap Proteins: Blocking the Road to Death's Door." *Nat Rev Mol Cell Biol* 3, no. 6 (2002): 401, Figure 1.

**Figure 4.2.5.7**

From Mattson, Mark P. "Apoptosis in Neurodegenerative Disorders." *Nat Rev Mol Cell Biol*, 1, no. 2 (2000): 120, Figure 2b.

**Figure 4.2.5.8**

From Youle, Richard J., and Mariusz Karbowski. "Mitochondrial Fission in Apoptosis."  
*Nat Rev Mol Cell Biol* 6, no. 8 (2005): 657, Figure 1.

A

B

**Figure 4.2.5.9**

A: from Jesenberger, Veronika, and Stefan Jentsch. "Deadly Encounter: Ubiquitin Meets Apoptosis." *Nat Rev Mol Cell Biol* 3, no. 2 (2002): 112, Box 1;

B: from Hipfner, David R., and Stephen M. Cohen. "Connecting Proliferation and Apoptosis in Development and Disease." *Nat Rev Mol Cell Biol* 5, no. 10 (2004): 805, Figure 2.

A

B

**Figure 4.2.5.10**

A: from Holcik, Martin, and Nahum Sonenberg. "Translational Control in Stress and Apoptosis." *Nat Rev Mol Cell Biol* 6, no. 4 (2005): 318, Box 2;

B: from Jin, Can, and John C. Reed. "Yeast and Apoptosis." *Nat Rev Mol Cell Biol* 3, no. 6 (2002): 453, Figure 1.



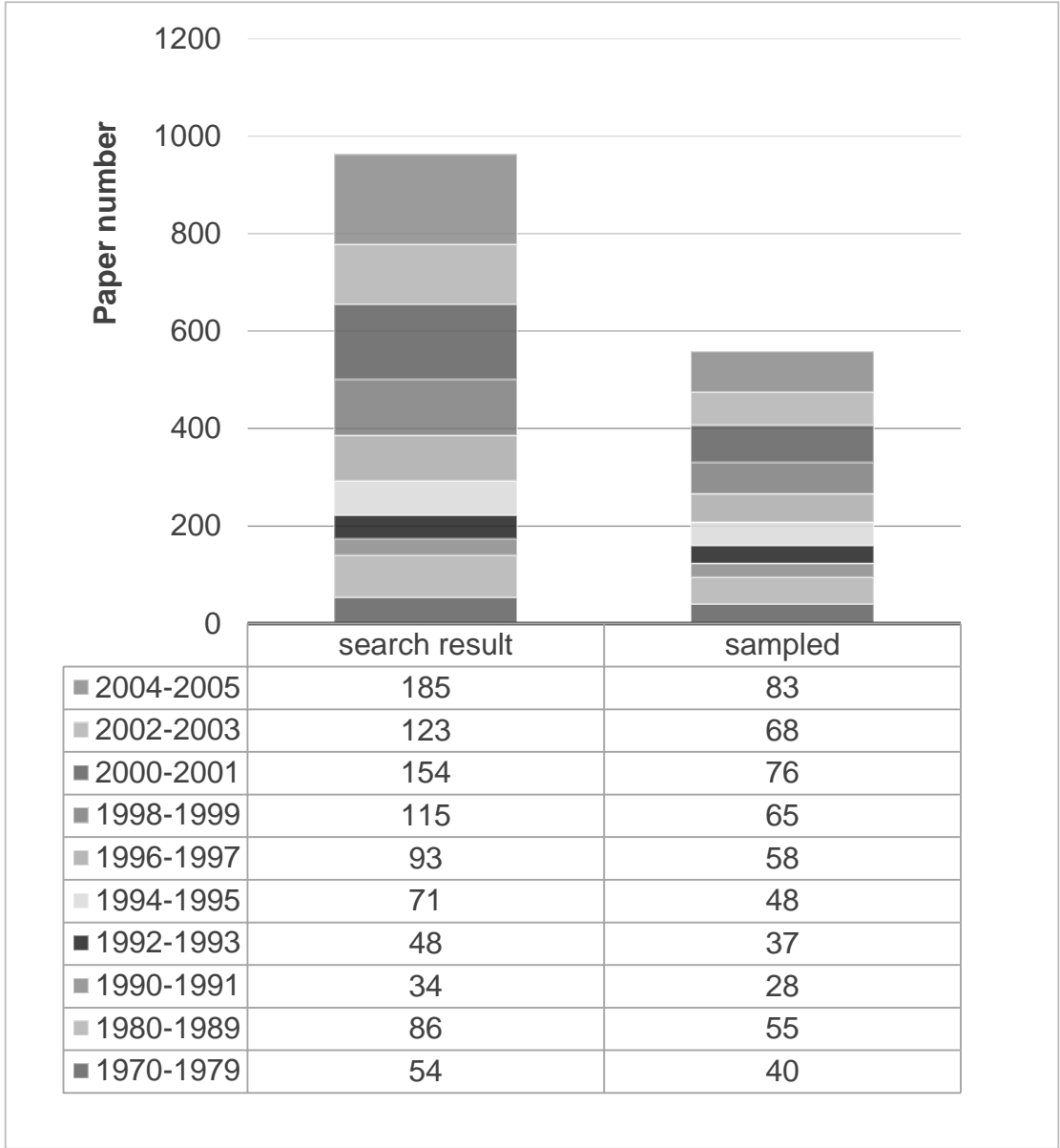
A

B

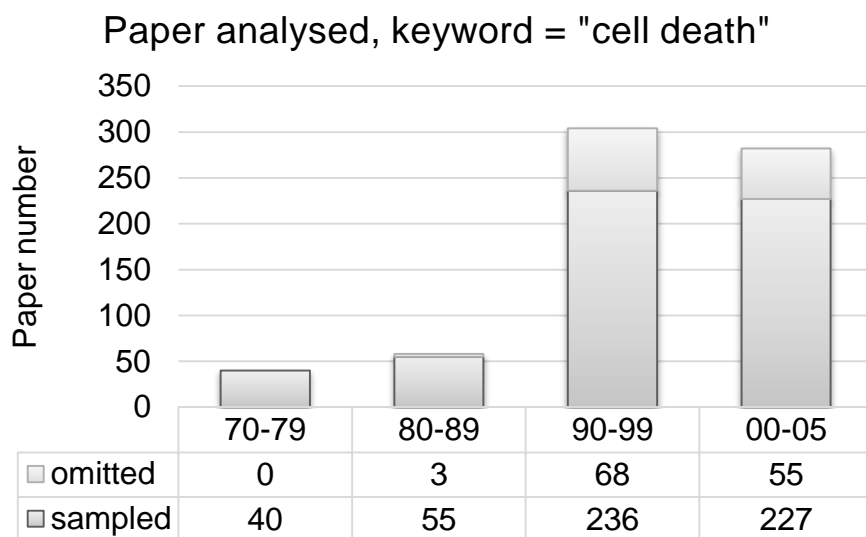
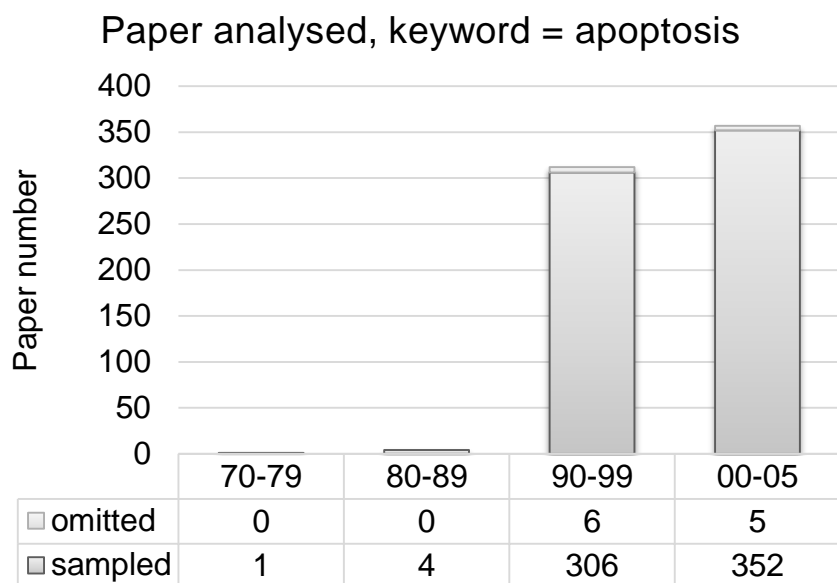
**Figure 4.2.5.11**

A: from Moncada, Salvador, and Jorge D. Erusalimsky. "Does Nitric Oxide Modulate Mitochondrial Energy Generation and Apoptosis?" *Nat Rev Mol Cell Biol* 3, no. 3 (2002): 214, Figure 2;

B: from Chipuk, Jerry E., and Douglas R. Green. "Do Inducers of Apoptosis Trigger Caspase-Independent Cell Death?" *Nat Rev Mol Cell Biol* 6, no. 3 (2005): 268, Box 2.

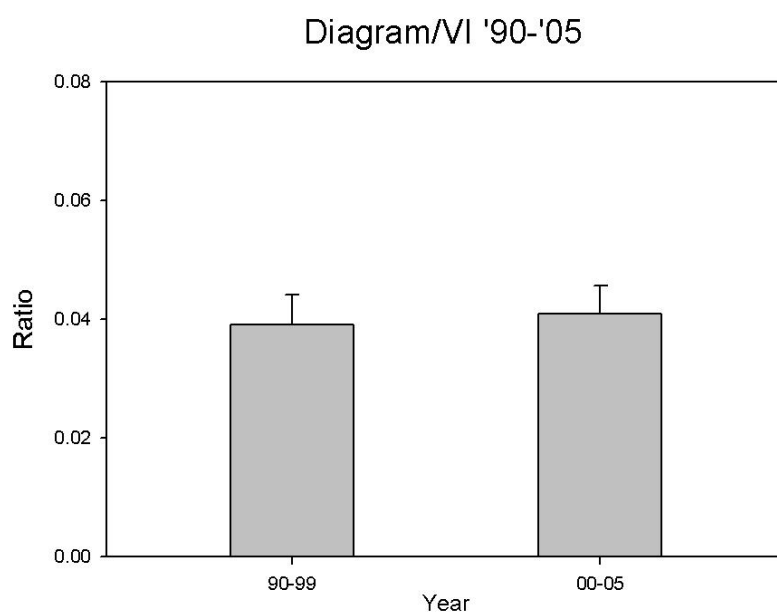


**Figure 4.2.6.1**  
Data profile of *Cancer Research*: search results and sampled papers shown in every two years.

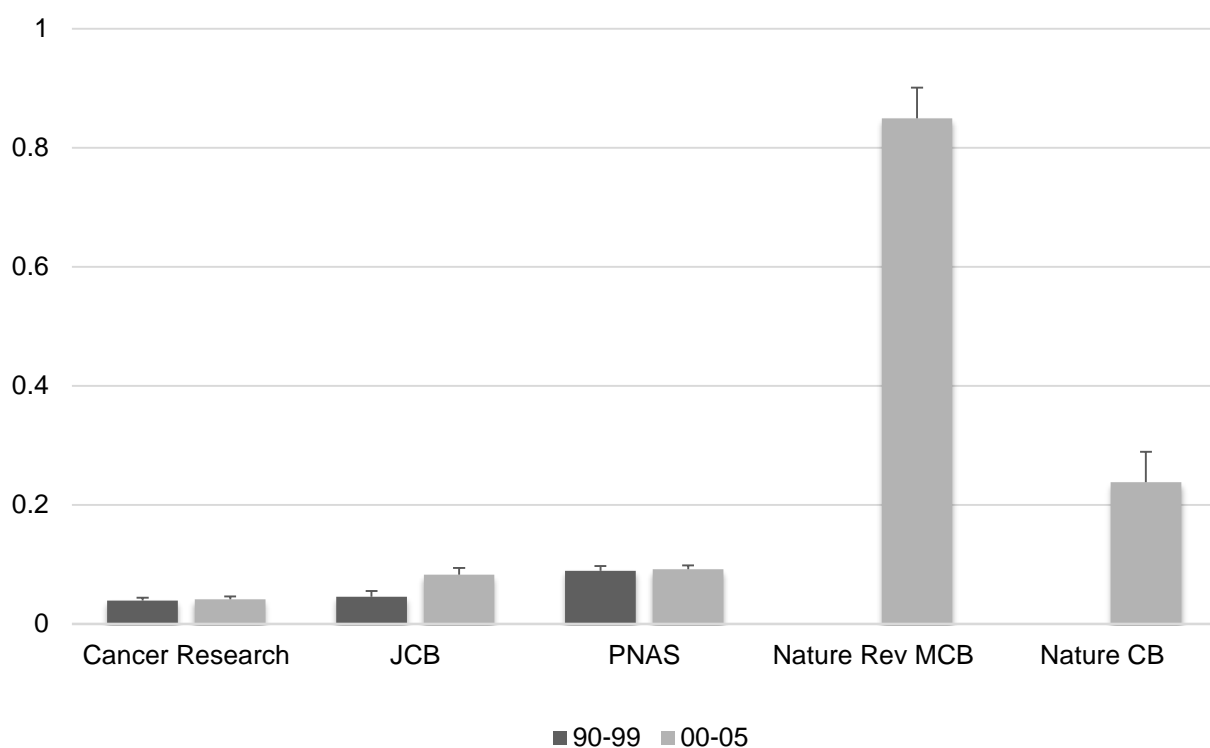


**Figure 4.2.6.2**

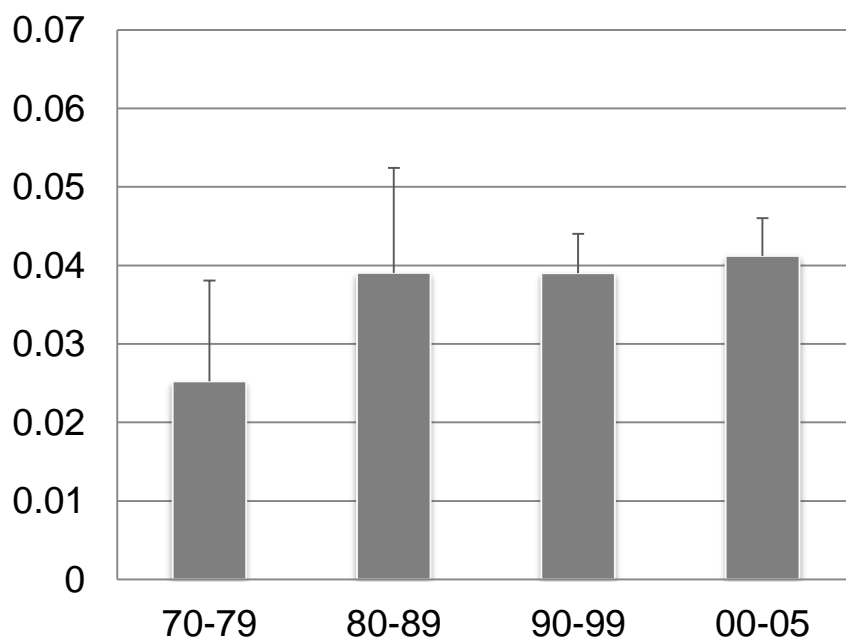
Data profile of *Cancer Research*: sampled and omitted papers in each decade.



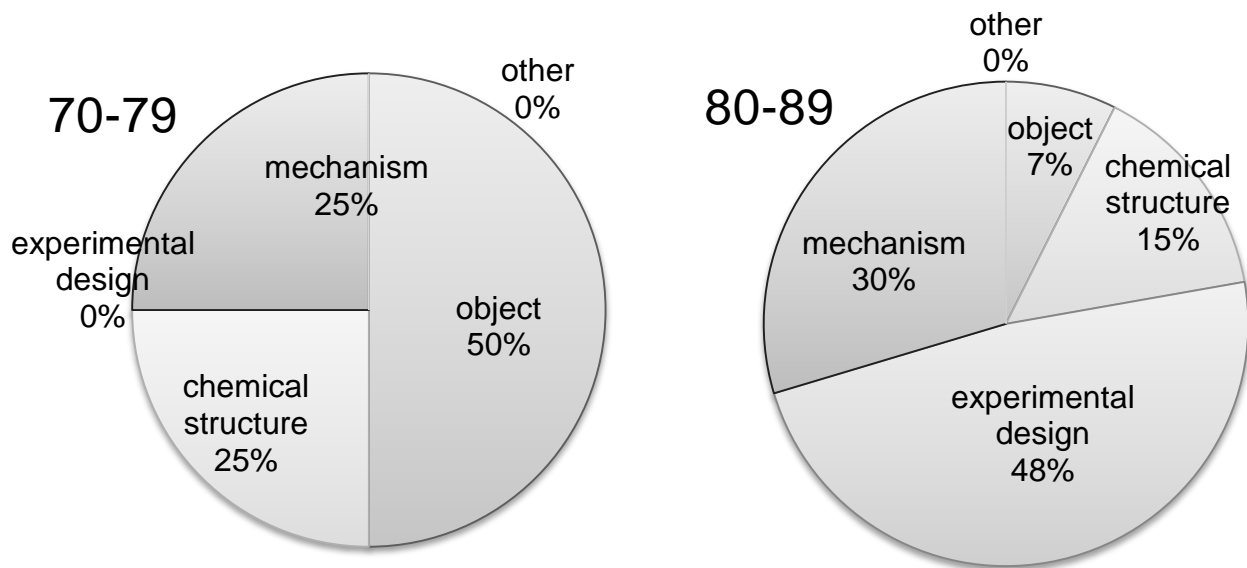
**Figure 4.2.6.3**  
D/VIs in *Cancer Research*, 1990–2005.



**Figure 4.2.6.4**  
Comparison: D/Vis in five journals, 1990–2005.

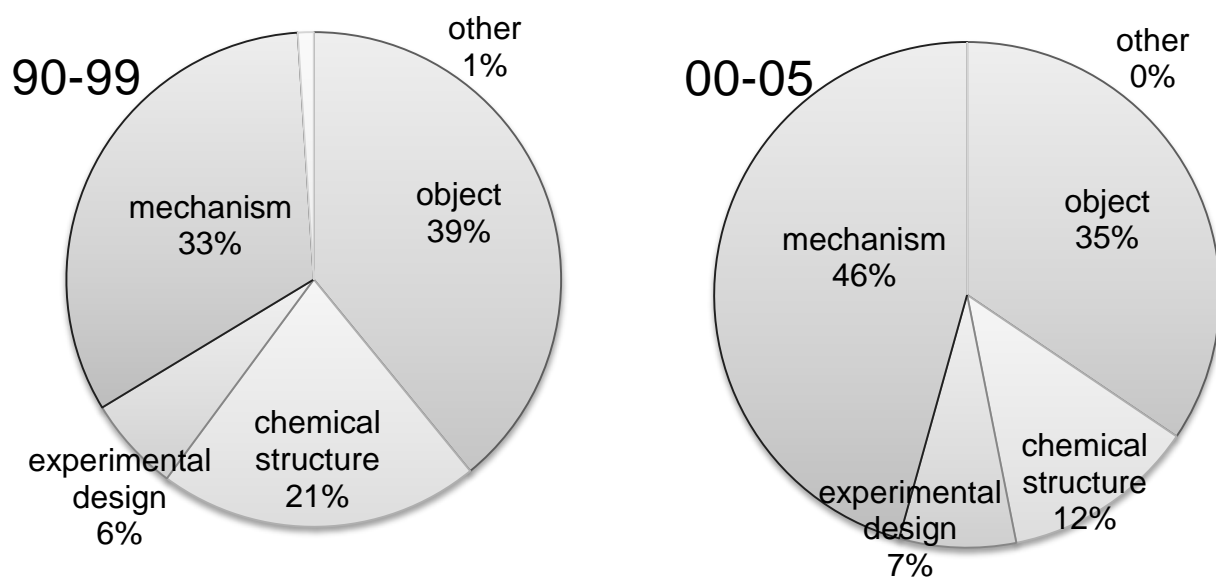


**Figure 4.2.6.5**  
D/VIs in *Cancer Research*, 1970–2005.



**Figure 4.2.6.6**

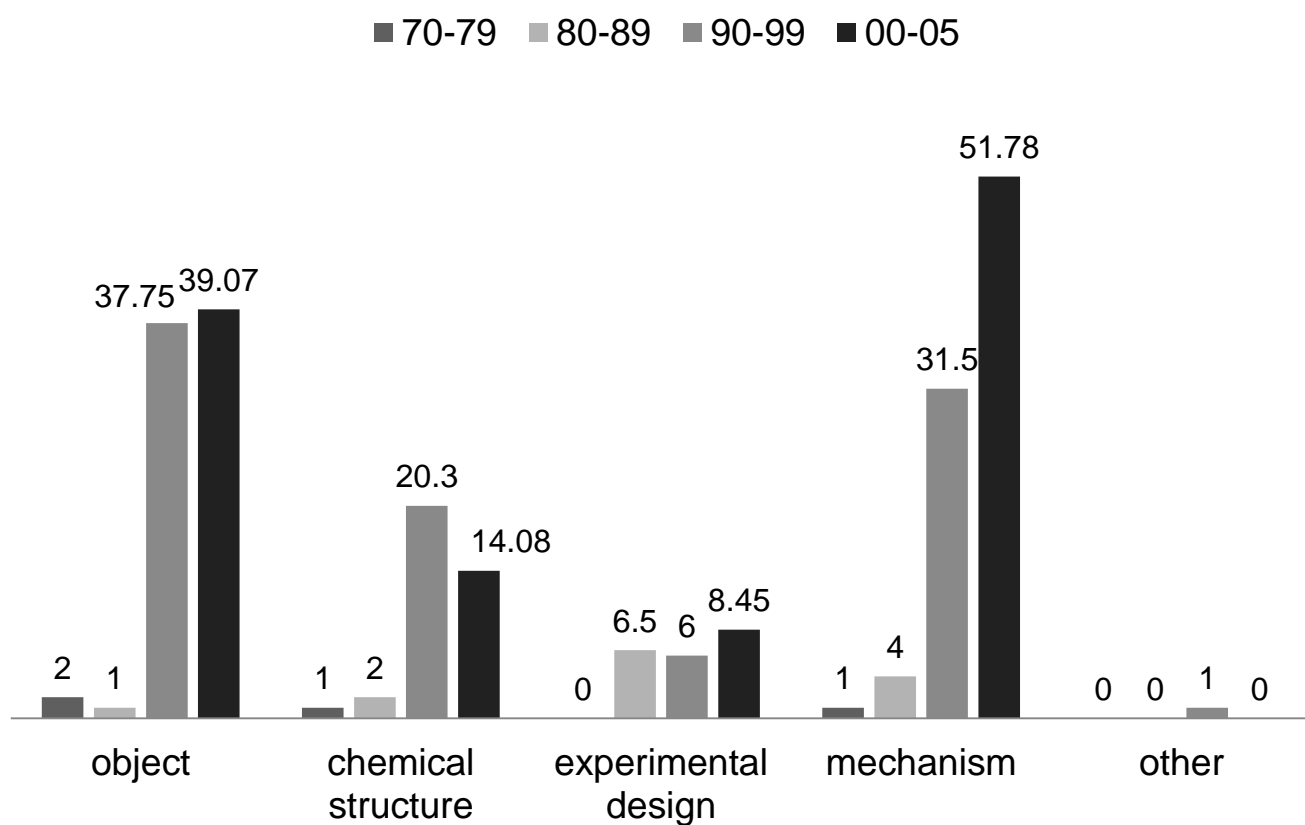
Proportions of diagram types in *Cancer Research*: 1970–1989.



**Figure 4.2.6.7**

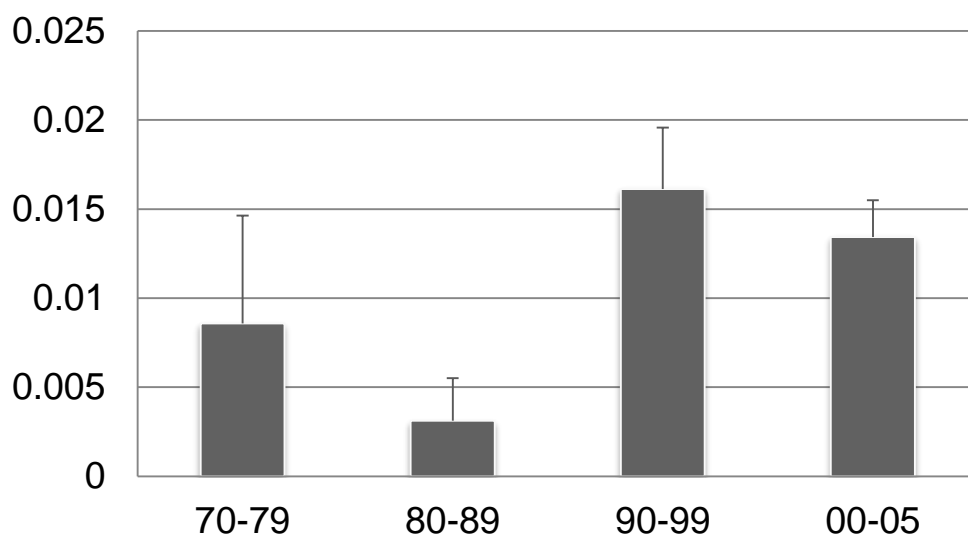
Proportions of diagram types in *Cancer Research*: 1990–2005.





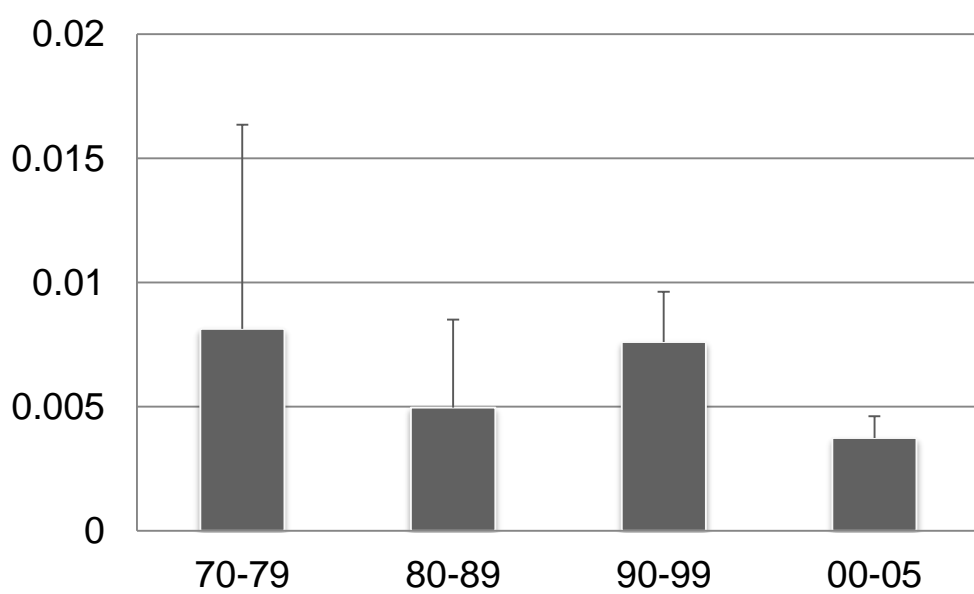
**Figure 4.2.6.8**

Numbers of five types of diagrams in each decade, 1970–2005.



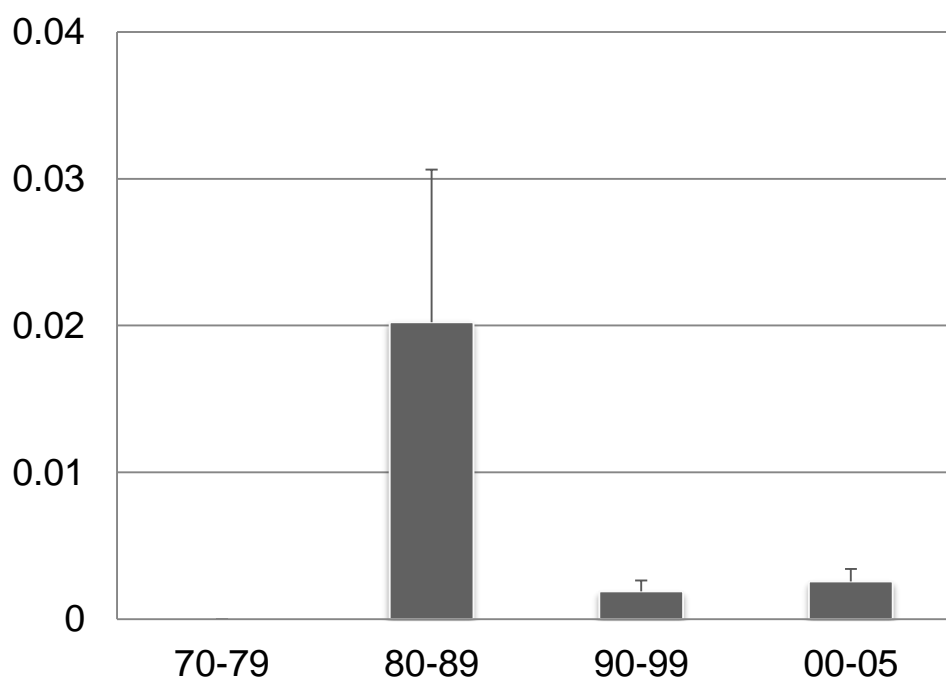
**Figure 4.2.6.9**

D/VIs of object diagrams, 1970–2005.



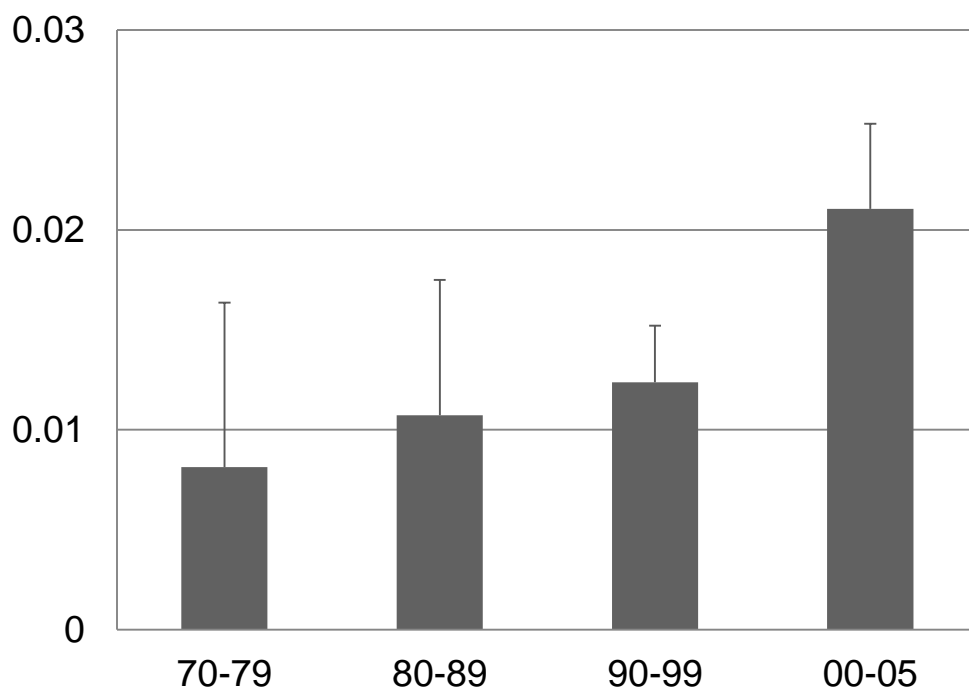
**Figure 4.2.6.10**

D/VIs of chemical structure diagrams, 1970–2005.



**Figure 4.2.6.11**

D/VIs of experimental design diagrams, 1970–2005.



**Figure 4.2.6.12**

D/VIs of mechanism diagrams, 1970–2005.

**A**

**B**

**Figure 4.2.6.13**

Object type. A: from Haji-Karim, Mohammed, and Jörgen Carisson. "Proliferation and Viability in Cellular Spheroids of Human Origin." *Cancer Research* 38, no. 5 (1978): 1457-64, Chart 1;

B: from Whitehead, James S., Frank J. Fearney, and Young S. Kim. "Glycosyltransferase and Glycosidase Activities in Cultured Human Fetal and Colonic Adenocarcinoma Cell Lines." *Cancer Research* 39, no. 4 (1979): 1259-63, Chart 1.

**A**

**B**

**Figure 4.2.6.14**

Object type. A: from Roth, Judith, Claudia Lenz-Bauer, Ana Contente, Kristina Löhr, Philipp Koch, Sandra Bernard, and Matthias Dobbelstein. "Reactivation of Mutant P53 by a One-Hybrid Adaptor Protein." *Cancer Research* 63, no. 14 (2003): 3904-08, Figure 1C;

B: from Kataoka, Hiromi, Paul Bonnefin, Diego Vieyra, Xiaolan Feng, Yasuo Hara, Yutaka Miura, Takashi Joh, Hidekazu Nakabayashi, Homayoun Vaziri, Curtis C. Harris, and Karl Riabowol. "Ing1 Represses Transcription by Direct DNA Binding and through Effects on P53." *Cancer Research* 63, no. 18 (2003): 5785-92, Figure 8.

**Figure 4.2.6.15**

Object type. From Zhang, Lei, Warren J. Gasper, Sanford A. Stass, Olga B. Ioffe, Myrtle A. Davis, and A. James Mixson. "Angiogenic Inhibition Mediated by a Dnzyme That Targets Vascular Endothelial Growth Factor Receptor 2." *Cancer Research* 62, no. 19 (2002): 5463-69, Figure 1B.



**Figure 4.2.6.16**

Object type. From Lou, Zhenjun, Sandra O'Reilly, Hongyan Liang, Veronica M. Maher, Stuart D. Sleight, and J. Justin McCormick. "Down-Regulation of Overexpressed Sp1 Protein in Human Fibrosarcoma Cell Lines Inhibits Tumor Formation." *Cancer Research* 65, no. 3 (2005): 1007-17, Figure 1C, D.

**Figure 4.2.6.17**

Experimental design type. From Li, Gang, Kapaettu Satyamoorthy, and Meenhard Herlyn. "N-Cadherin-Mediated Intercellular Interactions Promote Survival and Migration of Melanoma Cells." *Cancer Research* 61, no. 9 (2001): 3819-25, Figure 6A.

**A**

**B**

**Figure 4.2.6.18**

Experimental design type. A: from Kramer, Gero, Hamdiye Erdal, Helena J. M. M. Mertens, Marius Nap, Julian Mauermann, Georg Steiner, Michael Marberger, Kenneth Bivén, Maria C. Shoshan, and Stig Linder. "Differentiation between Cell Death Modes Using Measurements of Different Soluble Forms of Extracellular Cytokeratin 18." *Cancer Research* 64, no. 5 (2004): 1751-56, Figure 1;

B: from Eki, Toshihiko, Takemi Enomoto, Yasufumi Murakami, Fumio Hanaoka, and Masa-atsu Yamada. "Characterization of Chromosome Aberrations Induced by Incubation at a Restrictive Temperature in the Mouse Temperature-Sensitive Mutant tsFT20 Strain Containing Heat-Labile DNA Polymerase  $\alpha$ ." *Cancer Research* 47, no. 19 (1987): 5162-70, Figure 6.

**Figure 4.2.6.19**

“Other” type. From Vidair, Charles A., Chang H. Chen, Clifton C. Ling, and William C. Dewey. "Apoptosis Induced by X-Irradiation of Rec-Myc Cells Is Postmitotic and Not Predicted by the Time after Irradiation or Behavior of Sister Cells." *Cancer Research* 56, no. 18 (1996): 4116-18, Figure 1.

**Figure 4.2.6.20**

Mechanism type. From Hashimoto, Hisako, Satadal Chatterjee, and Nathan A. Berger. "Inhibition of Etoposide (Vp-16)-Induced DNA Recombination and Mutant Frequency by Bcl-2 Protein Overexpression." *Cancer Research* 55, no. 18 (1995): 4029-35, Figure 8.



**Figure 4.2.6.21**

Mechanism type. A: from Crowther, Penelope J., Ian A. Cooper, and David M. Woodcock. "Biology of Cell Killing by 1- $\beta$ -D-Arabinofuranosylcytosine and Its Relevance to Molecular Mechanisms of Cytotoxicity." *Cancer Research* 45, no. 9 (1985): 4291-300, Chart 4;

B: from Hirota, Yasuhide, Akiko Yoshioka, Shohei Tanaka, Kazuyo Watanabe, Takeshi Otani, Jun Minowada, Akira Matsuda, Tohru Ueda, and Yusuke Wataya. "Imbalance of Deoxyribonucleoside Triphosphates, DNA Double-Strand Breaks, and Cell Death Caused by 2-Chlorodeoxyadenosine in Mouse Fm3a Cells." *Cancer Research* 49, no. 4 (1989): 915-19, Figure 7.

**Figure 4.2.6.22**

Mechanism type. From Tannock, Ian F., and Daniela Rotin. "Acid Ph in Tumors and Its Potential for Therapeutic Exploitation." *Cancer Research* 49, no. 16 (1989): 4373-84, Figure 3.

**A**

**B**

**Figure 4.2.6.23**

Mechanism type. Both from Schulte-Hermann, Rolf, Irene Timmermann-Trosiener, Gertrud Barthel, and Wilfried Bursch. "DNA Synthesis, Apoptosis, and Phenotypic Expression as Determinants of Growth of Altered Foci in Rat Liver During Phenobarbital Promotion." *Cancer Research* 50, no. 16 (1990): 5127-35, A: Figure 1; B: Figure 12.



**A**

**B**

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**Figure 4.2.6.24**

Mechanism type. A: From Alnemri, Emad S., Teresa F. Fernandes, Subrata Haldar, Carlo M. Croce, and Gerald Litwack. "Involvement of Bcl-2 in Glucocorticoid-Induced Apoptosis of Human Pre-B-Leukemiasfr1]." *Cancer Research* 52, no. 2 (1992): 491-95, Figure 4;

B: from Ghose, Aurnab, Janis Fleming, Karam El-Bayoumy, and Paul R. Harrison. "Enhanced Sensitivity of Human Oral Carcinomas to Induction of Apoptosis by Selenium Compounds: Involvement of Mitogen-Activated Protein Kinase and Fas Pathways." *Cancer Research* 61, no. 20 (2001): 7479-87, Figure 2.

**Figure 4.2.6.25**

Mechanism type. From Waxman, David J., and Pamela S. Schwartz. "Harnessing Apoptosis for Improved Anticancer Gene Therapy." *Cancer Research* 63, no. 24 (2003): 8563-72, Figure 1.

**Figure 4.2.6.26**

Mechanism type. From Heinemann, Volker, Yi-Zheng Xu, Sherri Chubb, Alina Sen, Larry W. Hertel, Gerald B. Grindey, and William Plunkett. "Cellular Elimination of 2', 2'-Difluorodeoxycytidine 5'-Triphosphate: A Mechanism of Self-Potentialiation." *Cancer Research* 52, no. 3 (1992): 533-39, Figure 8.

**Figure 4.2.6.27**

Mechanism type. From Hiraku, Yusuke, and Shosuke Kawanishi. "Oxidative DNA Damage and Apoptosis Induced by Benzene Metabolites." *Cancer Research* 56, no. 22 (1996): 5172-78, Figure 10.

**Figure 4.2.6.28**

Mechanism type. From Walton, M. I., D. Whyson, P. M. O'Connor, D. Hockenbery, S. J. Korsmeyer, and K. W. Kohn. "Constitutive Expression of Human Bcl-2 Modulates Nitrogen Mustard and Camptothecin Induced Apoptosis." *Cancer Research* 53, no. 8 (1993): 1853-61, Figure 6.

**Figure 4.2.6.29**

Mechanism type. From Lemonnier, Loïc, Yaroslav Shuba, Alexandre Crepin, Morad Roudbaraki, Christian Slomianny, Brigitte Mauroy, Bernd Nilius, Natalia Prevarskaya, and Roman Skryma. "Bcl-2-Dependent Modulation of Swelling-Activated Cl<sup>-</sup> Current and Clc-3 Expression in Human Prostate Cancer Epithelial Cells." *Cancer Research* 64, no. 14 (2004): 4841-48, Figure 7.

**Figure 4.2.6.30**

Mechanism type. From Xiao, Danhua, John T. Pinto, Jae-Won Soh, Atsuko Deguchi, Gregg G. Gundersen, Alexander F. Palazzo, Jung-Taek Yoon, Haim Shirin, and I. Bernard Weinstein. "Induction of Apoptosis by the Garlic-Derived Compound S-Allylmercaptocysteine (SAMC) Is Associated with Microtubule Depolymerization and C-Jun NH(2)-Terminal Kinase 1 Activation." *Cancer Research* 63, no. 20 (2003): 6825-37, Figure 9.

**Figure 4.2.6.31**

Mechanism type. From Colombel, Marc, Carl A. Olsson, Po-Ying Ng, and Ralph Buttyan. "Hormone-Regulated Apoptosis Results from Reentry of Differentiated Prostate Cells onto a Defective Cell Cycle." *Cancer Research* 52, no. 16 (1992): 4313-19, Figure 5.



**Figure 4.2.6.32**

Mechanism type. From Yamaguchi, Hirohito, Kapil Bhalla, and Hong-Gang Wang. "Bax Plays a Pivotal Role in Thapsigargin-Induced Apoptosis of Human Colon Cancer Hct116 Cells by Controlling Smac/Diablo and Omi/Htra2 Release from Mitochondria." *Cancer Research* 63, no. 7 (2003): 1483-89, Figure 6D.

**Figure 4.2.6.33**

Mechanism type. From Childs, April C., Sharon L. Phaneuf, Amie J. Dirks, Tracey Phillips, and Christiaan Leeuwenburgh. "Doxorubicin Treatment in Vivo Causes Cytochrome C Release and Cardiomyocyte Apoptosis, as Well as Increased Mitochondrial Efficiency, Superoxide Dismutase Activity, and Bcl-2:Bax Ratio." *Cancer Research* 62, no. 16 (2002): 4592-98, Figure 5.

**Figure 4.2.6.34**

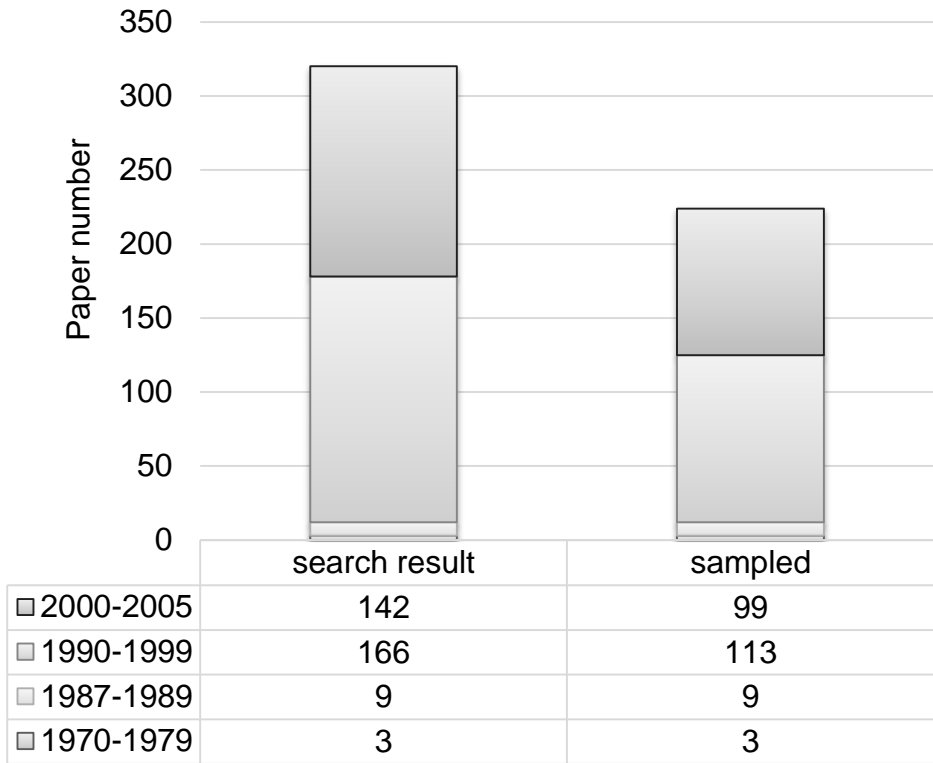
Mechanism type. From Benoit, Valérie, Alain Chariot, Laurence Delacroix, Valérie Deregowski, Nathalie Jacobs, Marie-Paule Merville, and Vincent Bours. "Caspase-8-Dependent Her-2 Cleavage in Response to Tumor Necrosis Factor  $\alpha$  Stimulation Is Counteracted by Nuclear Factor  $\kappa$ B through C-Flip-L Expression." *Cancer Research* 64, no. 8 (2004): 2684-91, Figure 11.

**Figure 4.2.6.35**

Mechanism type. From Horvitz, H. Robert. "Genetic Control of Programmed Cell Death in the Nematode *Caenorhabditis Elegans*." *Cancer Research* 59, no. 7 Supplement (1999): 1701s-06s, Figure 3.

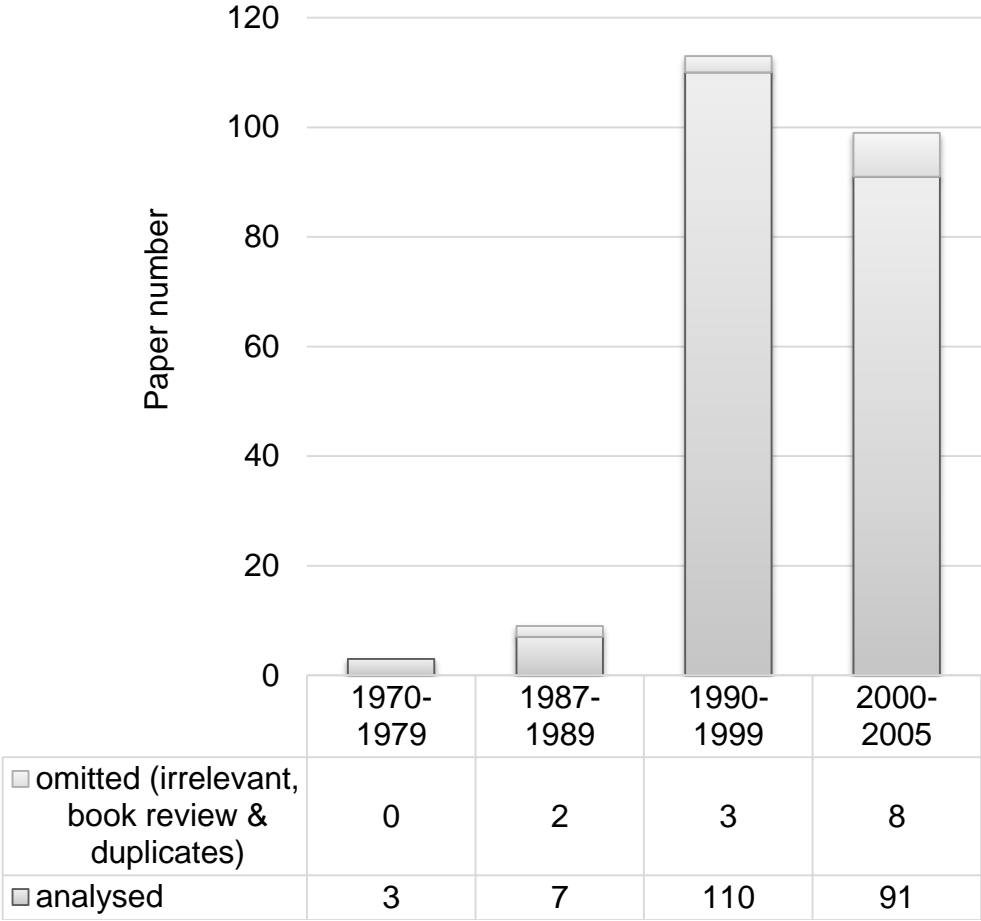
**Figure 4.2.6.36**

Mechanism type. From Korsmeyer, Stanley J. "Bcl-2 Gene Family and the Regulation of Programmed Cell Death." *Cancer Research* 59, no. 7 Supplement (1999): 1693s-700s, Figure 8.

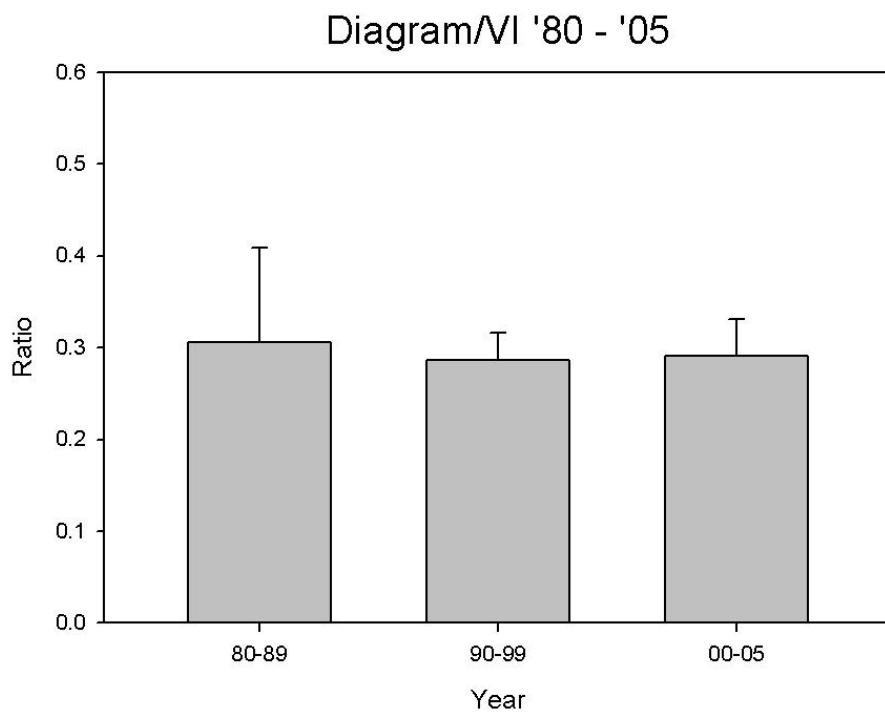


**Figure 4.2.7.1**

Data profile of *Cell*: search result and sampled.



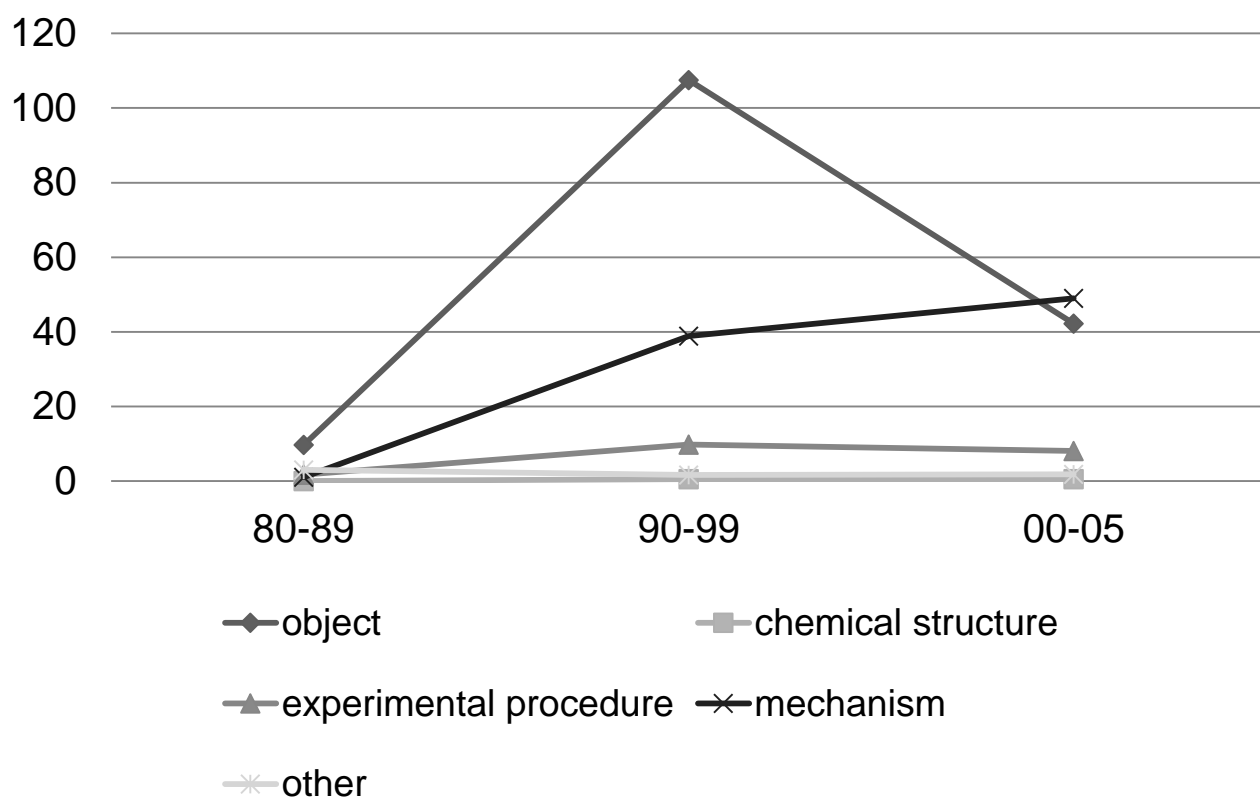
**Figure 4.2.7.2**  
Data profile of *Cell*: analysed and omitted papers.



**Figure 4.2.7.3**  
D/VI in *Cell* 1980s–2000s.

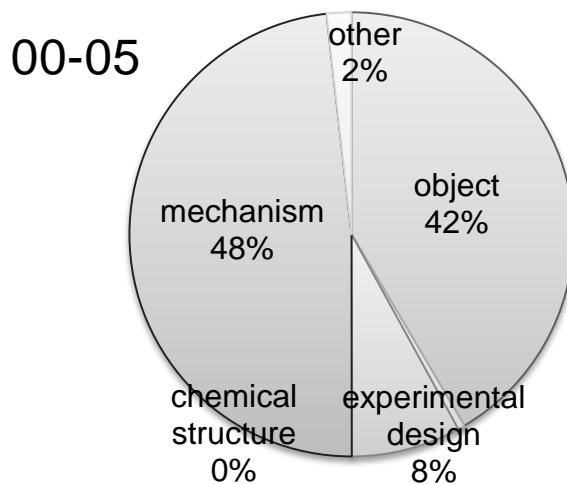
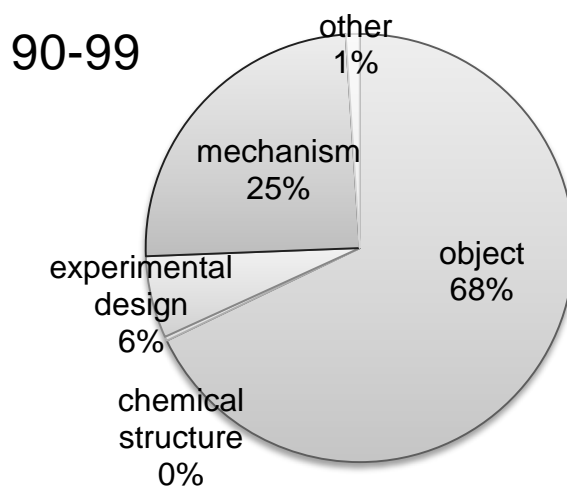
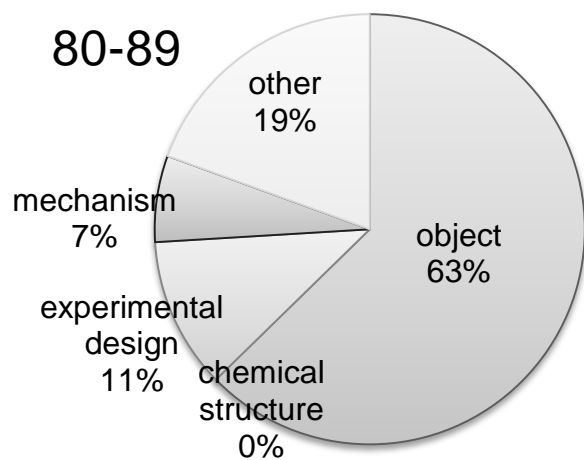


### Number of 5 types of diagram '80 -'05



**Figure 4.2.7.4**

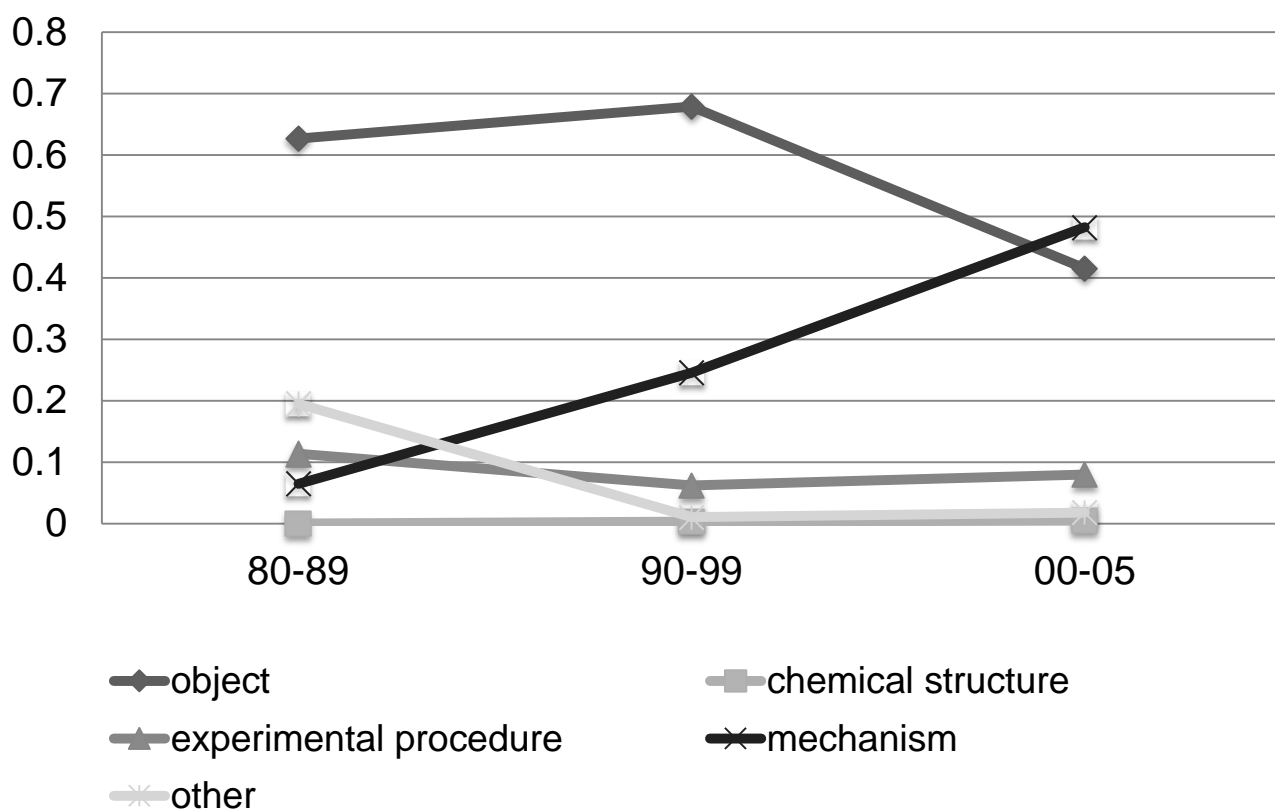
Changes in numbers of five diagram types in *Cell*, 1980–2005.



**Figure 4.2.7.5**

Changes in proportions of five diagram types in *Cell*, 1980–2005.

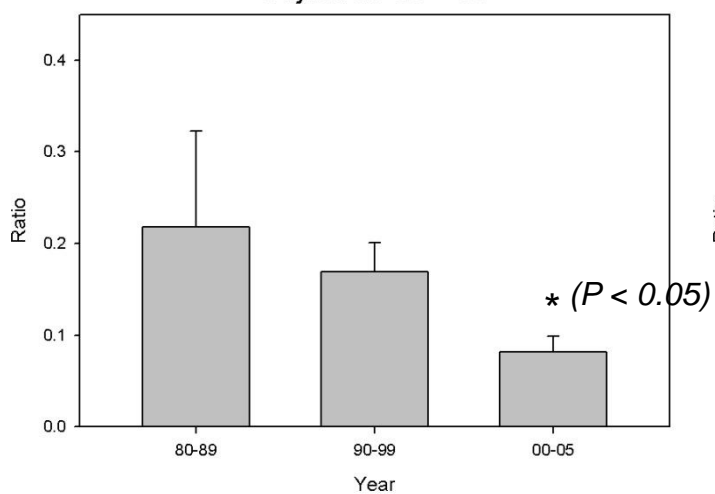
### Proportion of diagram types '80 - '05



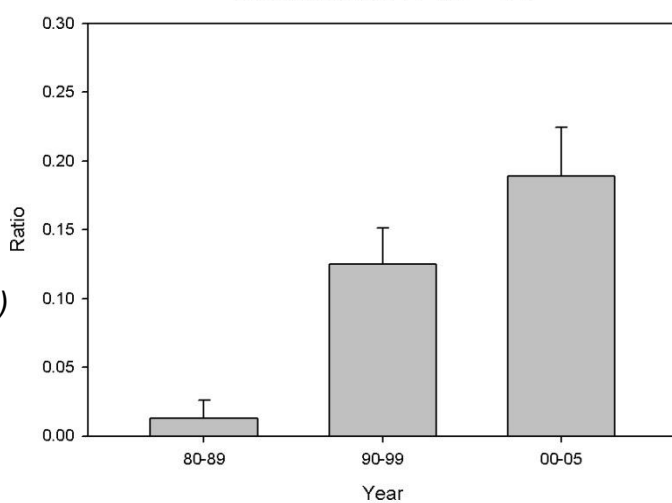
**Figure 4.2.7.6**

Changes in proportions of five diagram types in *Cell*, 1980–2005.

Object/VI '80 - '05



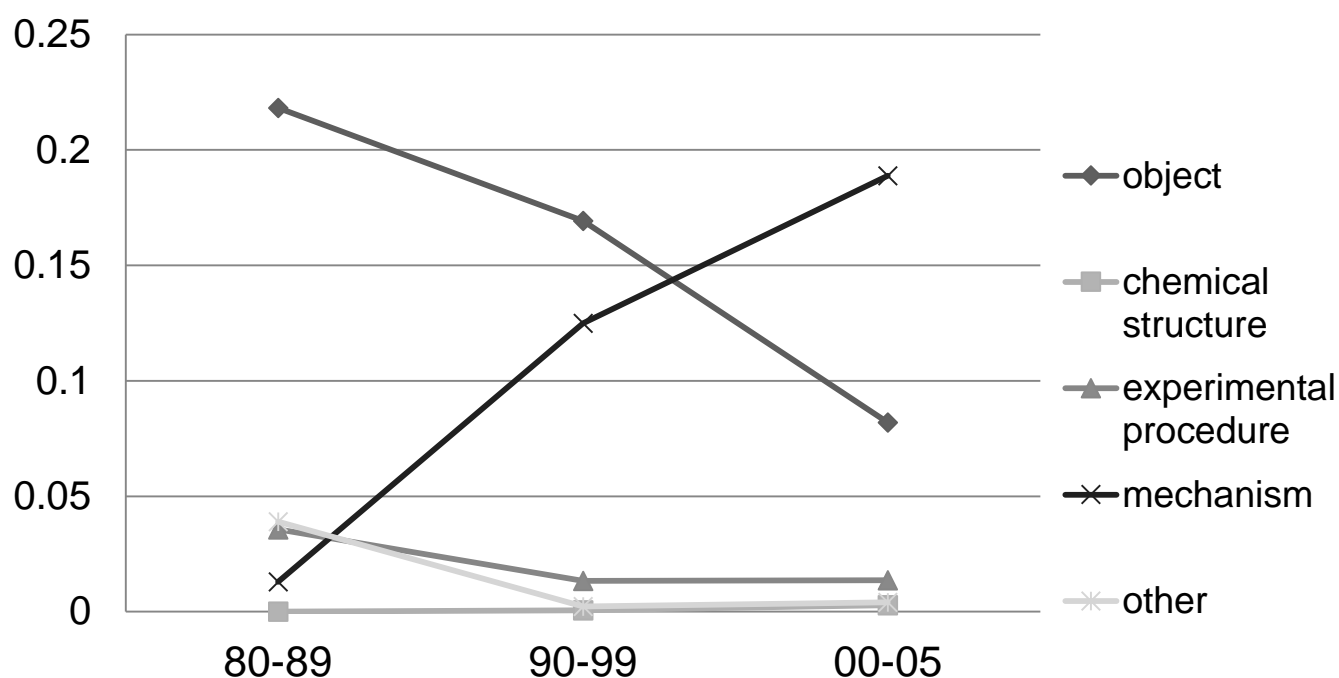
Mechanism/VI '80 - '05



**Figure 4.2.7.7**

D/VIs of two prevalent diagram types in *Cell*, 1980–2005.

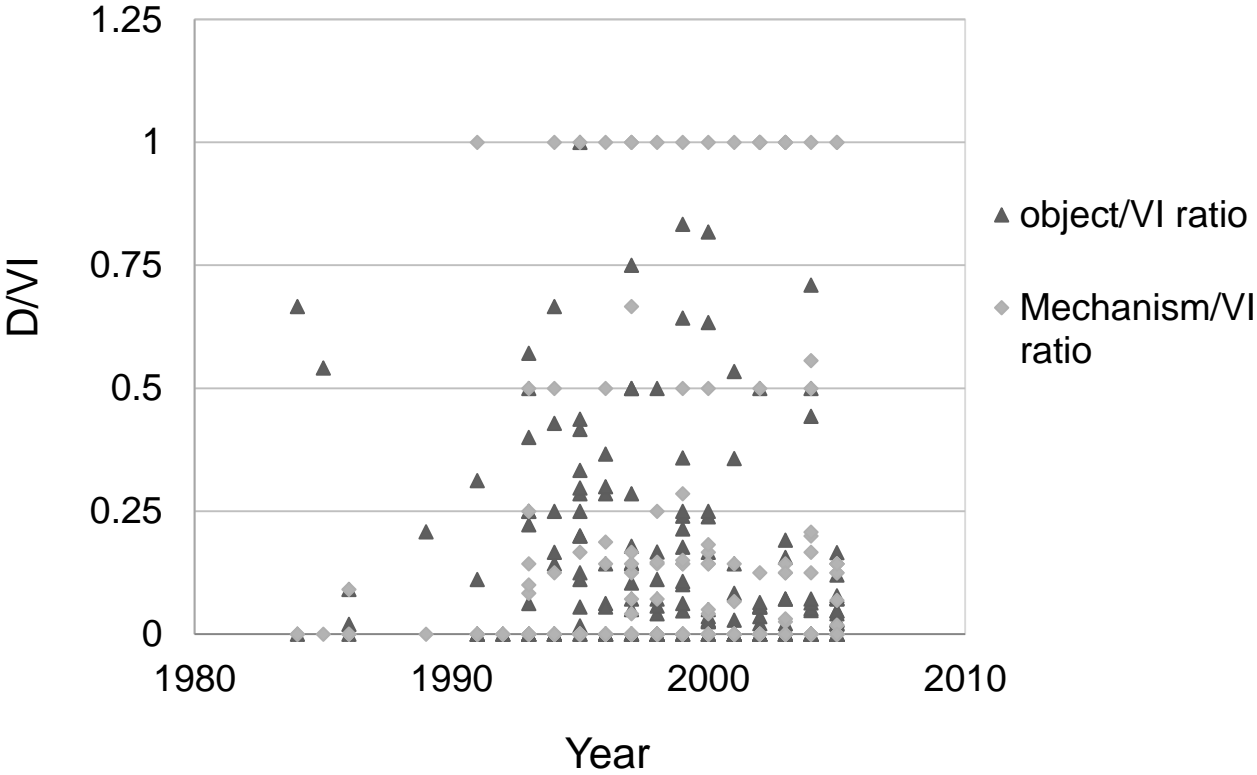
## D/VI of 5 diagram types '80 - '05



**Figure 4.2.7.8**

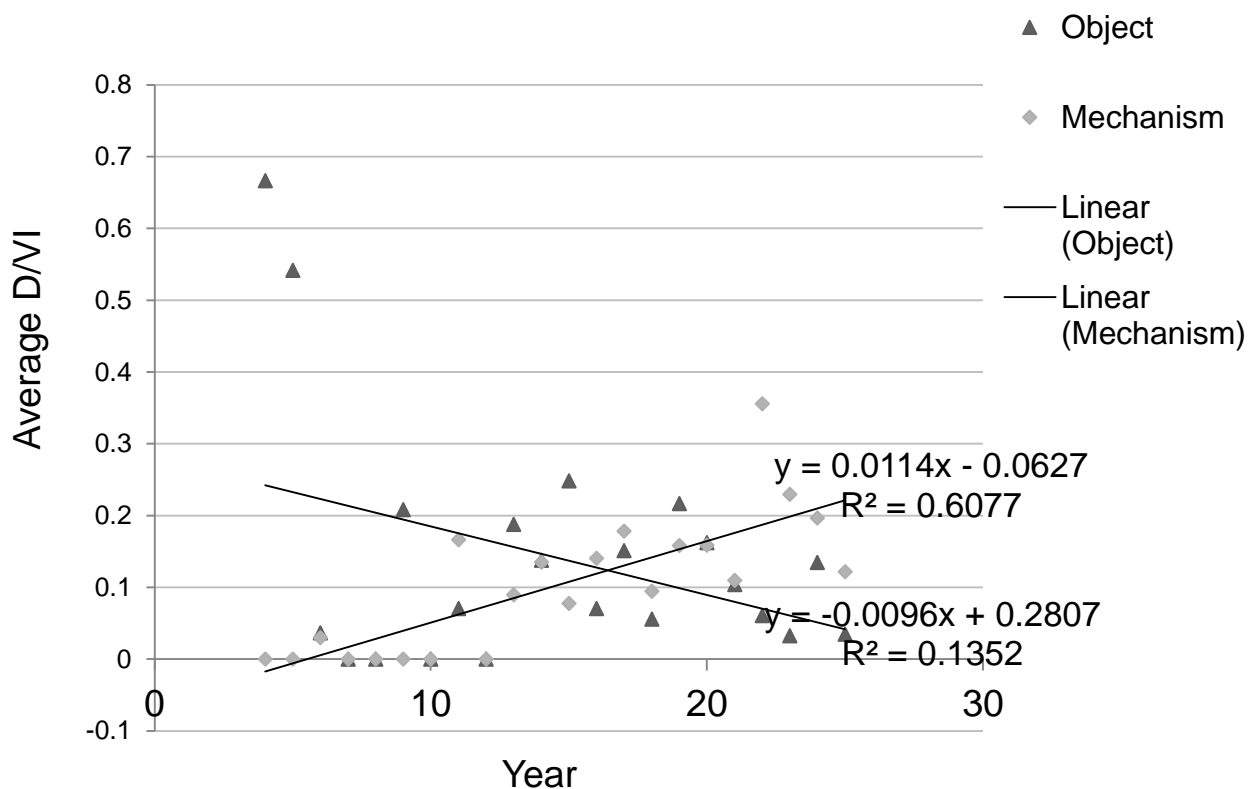
Changes in D/VI of different diagram types in *Cell*, 1980–2005 (1): average of each decade.

Object/VI & mechanism/VI '80 – '05



**Figure 4.2.7.9**  
Changes in D/VI of two prevalent diagram types in *Cell*, 1980–2005 (2): scatter plotting.

## Average object/VI & mechanism/VI '80 - '05

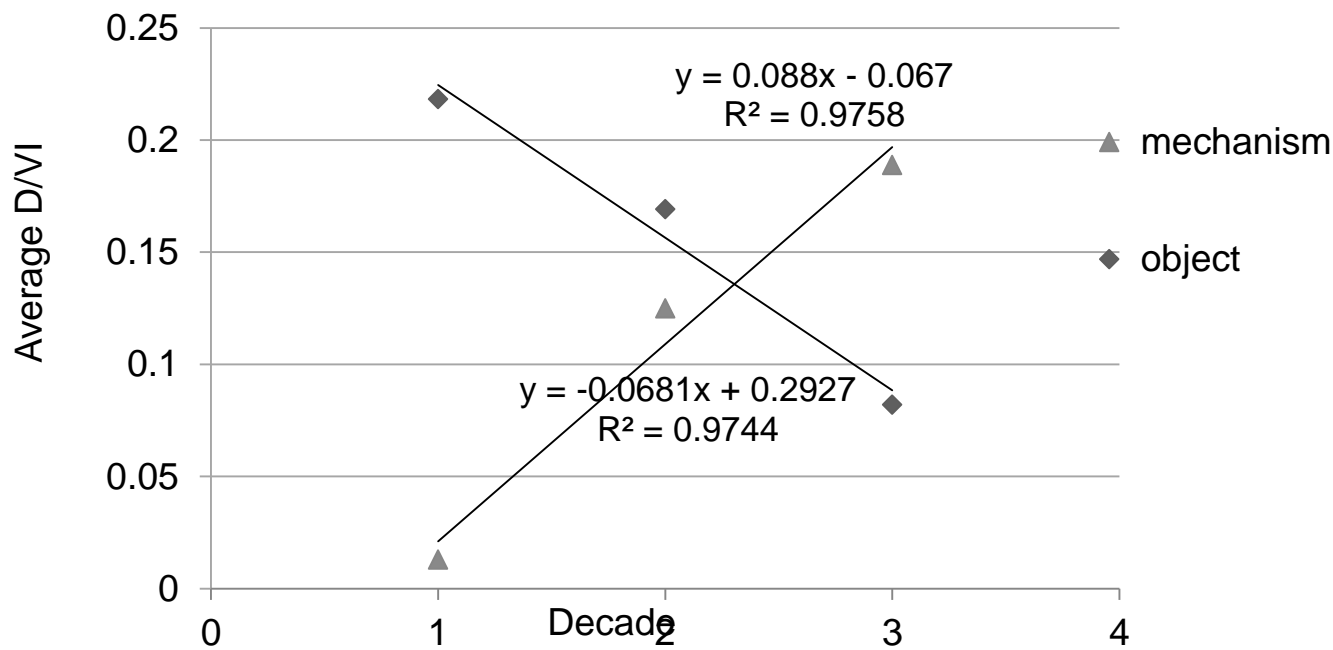


**Figure 4.2.7.10**

Changes in D/VI of two prevalent types in *Cell*, 1980–2005 (3): scatter plotting of average numbers, trend lines, and regression analyses.

Note: the baseline of year axis is 1980.

**Average object/VI & mechanism/VI 80s, 90s, 00s**



**Figure 4.2.7.11**  
Changes in D/VI of two prevalent types in *Cell*, 1980–2005 (4):  
average D/VIs, trend lines, and regression analyses.  
Note: decade 1980 is assigned as 1, 1990s = 2, 2000s = 3.



**A**

**B**

**C**

**Figure 4.2.7.12**

Object type.

A: from Vu, Thiennu H., J. Michael Shipley, et al. "Mmp-9/Gelatinase B Is a Key Regulator of Growth Plate Angiogenesis and Apoptosis of Hypertrophic Chondrocytes." *Cell* 93, no. 3 (1998): 411-22, Figure 2A;

B: from Coucouvanis, Electra, and Gail R. Martin. "Signals for Death and Survival: A Two-Step Mechanism for Cavitation in the Vertebrate Embryo." *Cell* 83, no. 2 (1995): 279-87, Figure 1A;

C: from Hodgkin, Jonathan. "Sex, Cell Death, and the Genome of *C. Elegans*." *Cell* 98, no. 3 (1999): 277-80, Figure 1.



**Figure 4.2.7.13**

Object type.

Left: from Lohmann, Ingrid, Nadine McGinnis, et al. "The Drosophila Hox Gene Deformed Sculpts Head Morphology Via Direct Regulation of the Apoptosis Activator Reaper." *Cell* 110, no. 4 (2002): 457-66, figure 1;

Right: from Baker, Nicholas E., and Sung-Yun Yu. "The Egf Receptor Defines Domains of Cell Cycle Progression and Survival to Regulate Cell Number in the Developing Drosophila Eye." *Cell* 104, no. 5 (2001): 699-708, Figure 7.

**Figure 4.2.7.14**

Object type. From Jacobson, Michael D., Miguel Weil, et al. "Programmed Cell Death in Animal Development." *Cell* 88, no. 3 (1997): 347-54, Figure 2.



**Figure 4.2.7.15**

Left: Object type. Right: the icon embedded in a diagram of experimental design. Left: from Bagri, Anil, Hwai-Jong Cheng, et al. "Stereotyped Pruning of Long Hippocampal Axon Branches Triggered by Retraction Inducers of the Semaphorin Family." *Cell* 113, no. 3 (2003): 285-99, figure 1A; right: Figure 4A from the same paper.

**Figure 4.2.7.16**

Object type. *Ibid*, Figure 4H-K.

**A**

**B**

**C**

**D**

**Figure 4.2.7.17**

Experimental design type.

A: from Epping, Mirjam T., Liming Wang, et al. "The Human Tumor Antigen Prame Is a Dominant Repressor of Retinoic Acid Receptor Signaling." *Cell* 122, no. 6 (2005): 835-47, figure 2C;

B: from Kraus, Manfred, Marat B. Alimzhanov, et al. "Survival of Resting Mature B Lymphocytes Depends on Bcr Signaling Via the Ig $\pm$ /2 Heterodimer." *Cell* 117, no. 6 (2004): 787-800, figure 2A;

C: from Hieter, Philip, David Pridmore, et al. "Functional Selection and Analysis of Yeast Centromeric DNA." *Cell* 42, no. 3 (1985): 913-21, figure 1a;

D: from Glass, David J., Steven H. Nye, et al. "Trk13 Mediates Bdnf/Nt-3-Dependent Survival and Proliferation in Fibroblasts Lacking the Low Affinity Ngf Receptor." *Cell* 66, no. 2 (1991): 405-13, figure 2.

**A**

**B**

**Figure 4.2.7.18**

Experimental design type.

A: from Ikura, Tsuyoshi, Vasily V. Ogryzko, et al. "Involvement of the Tip60 Histone Acetylase Complex in DNA Repair and Apoptosis." *Cell* 102, no. 4 (2000): 463-73, Figure 5A;

B: from Quigley, John G., Zhantao Yang, et al. "Identification of a Human Heme Exporter That Is Essential for Erythropoiesis." *Cell* 118, no. 6 (2004): 757-66, figure 4.

**Figure 4.2.7.19**

Experimental design type. From Ricci, Jean-Ehrland, Cristina Muñoz-Pinedo, et al. "Disruption of Mitochondrial Function During Apoptosis Is Mediated by Caspase Cleavage of the P75 Subunit of Complex I of the Electron Transport Chain." *Cell* 117, no. 6 (2004): 773-86, figure 1A.



**A**

**B**

**C**

**D**

**Figure 4.2.7.20**

“Other” type. A: from Drewes, Gerard, Andreas Ebner, et al. "Mark, a Novel Family of Protein Kinases That Phosphorylate Microtubule-Associated Proteins and Trigger Microtubule Disruption." *Cell* 89, no. 2 (1997): 297-308, figure 1C; B: from Liu, Qiong A., and Michael O. Hengartner. "Candidate Adaptor Protein Ced-6 Promotes the Engulfment of Apoptotic Cells in *C. Elegans*." *Cell* 93, no. 6 (1998): 961-72, Figure 3C; C: from McGill, Gaël G., Martin Horstmann, et al. "Bcl2 Regulation by the Melanocyte Master Regulator Mitf Modulates Lineage Survival and Melanoma Cell Viability." *Cell* 109, no. 6 (2002): 707-18, Figure 1D; D: from Ellis, Hilary M., and H. Robert Horvitz. "Genetic Control of Programmed Cell Death in the Nematode *C. Elegans*." *Cell* 44, no. 6 (1986): 817-29, figure 3.

**Figure 4.2.7.21**

“Other” type. From Chabes, Andrei, Bilyana Georgieva, et al. "Survival of DNA Damage in Yeast Directly Depends on Increased Dntp Levels Allowed by Relaxed Feedback Inhibition of Ribonucleotide Reductase." *Cell* 112, no. 3 (2003): 391-401, Figure 5.

**Figure 4.2.7.22**

Mechanism type. From Ellis, Hilary M., and H. Robert Horvitz. "Genetic Control of Programmed Cell Death in the Nematode *C. Elegans*." *Cell* 44, no. 6 (1986): 817-29, Figure 10.

**A**

**B**

**Figure 4.2.7.23**

Mechanism diagrams that are visually similar to object diagrams. A: from Oda, Katsutoshi, Hirofumi Arakawa, et al. "P53aip1, a Potential Mediator of P53-Dependent Apoptosis, and Its Regulation by Ser-46-Phosphorylated P53." *Cell* 102, no. 6 (2000): 849-62, Figure 8E; B: from Conradt, Barbara, and H. Robert Horvitz. "The Tra-1a Sex Determination Protein of *C. Elegans* Regulates Sexually Dimorphic Cell Deaths by Repressing the Egl-1 Cell Death Activator Gene." *Cell* 98, no. 3 (1999): 317-27, Figure 5.

**A**

**B**

**C**

**Figure 4.2.7.24**

Mechanism diagrams that are visually similar to object diagrams.

A: from Liu, Zheng-gang, Hailing Hsu, et al. "Dissection of Tnf Receptor 1 Effector Functions: Jnk Activation Is Not Linked to Apoptosis While Nf- $\kappa$ B Activation Prevents Cell Death." *Cell* 87, no. 3 (1996): 565-76, Figure 1A;

B: Park, Young Chul, Hong Ye, et al. "A Novel Mechanism of Traf Signaling Revealed by Structural and Functional Analyses of the Tradd Traf2 Interaction." *Cell* 101, no. 7 (2000): 777-87, Figure 1D;

C: from Boldin, Mark P., Tanya M. Goncharov, et al. "Involvement of Mach, a Novel Mort1/Fadd-Interacting Protease, in Fas/Apo-1- and Tnf Receptor Induced Cell Death." *Cell* 85, no. 6 (1996): 803-15., Figure 7.

**Figure 4.2.7.25**

Mechanism type: an extravagant example. From Green, Douglas R. "Apoptotic Pathways: Ten Minutes to Dead." *Cell* 121, no. 5 (2005): 671-74, Figure 1.

**Figure 4.2.7.26**

Mechanism type: a case that is pictorial and very similar to the object type. From Shi, Yigong. "Caspase Activation: Revisiting the Induced Proximity Model." *Cell* 117, no. 7 (2004): 855-58, Figure 3.

**Figure 4.2.7.27**

A mechanism diagram containing various elements. Di Cristofano, Antonio, and Pier Paolo Pandolfi. "The Multiple Roles of Pten in Tumor Suppression." *Cell* 100, no. 4 (2000): 387-90, Figure 1.



#### **Figure 4.2.7.28**

A case of mechanism diagram: two forms of data images (photograph and chart) and a schematic diagram jointly illustrate a conceptual model. From Schumacher, Björn, Momoyo Hanazawa, et al. "Translational Repression of C. Elegans P53 by Gld-1 Regulates DNA Damage-Induced Apoptosis." *Cell* 120, no. 3 (2005): 357-68, Figure 6.

**Figure 4.2.7.29**

Mechanism type. From Abrams, John M. "Competition and Compensation: Coupled to Death in Development and Cancer." *Cell* 110, no. 4 (2002): 403-06, Figure 1.

**A**

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**B**

**Figure 4.2.7.30**

Mechanism type.

A: From Ravichandran, Kodi S. "Recruitment Signals from Apoptotic Cells: Invitation to a Quiet Meal." *Cell* 113, no. 7 (2003): 817-20;

B: as cited in Figure 4.2.6.35.

**Figure 4.2.7.31**

Mechanism type. From Fesik, Stephen W. "Insights into Programmed Cell Death through Structural Biology." *Cell* 103, no. 2 (2000): 273-82, Figure 7.



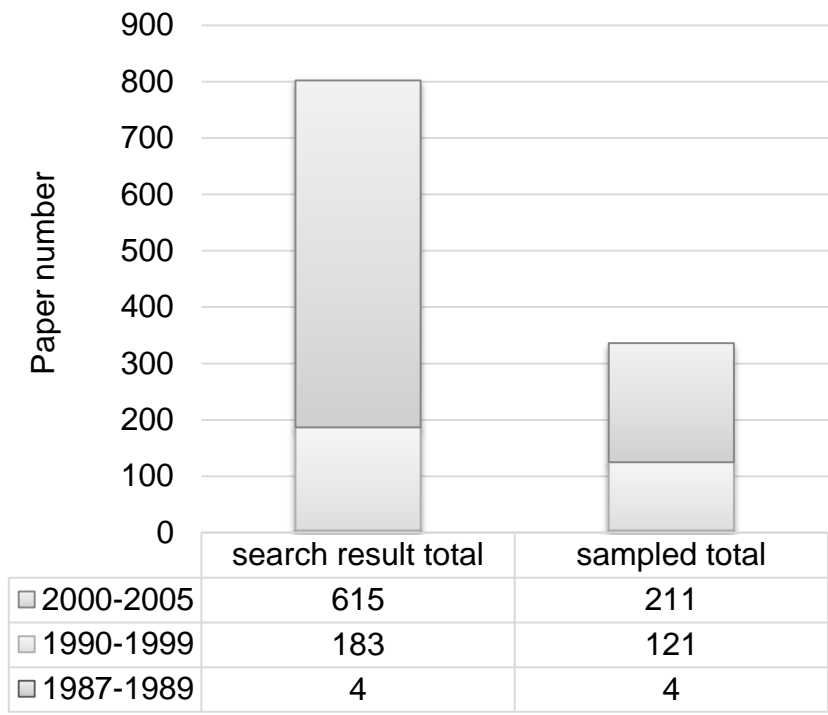
**Figure 4.2.7.32**

Mechanism type.

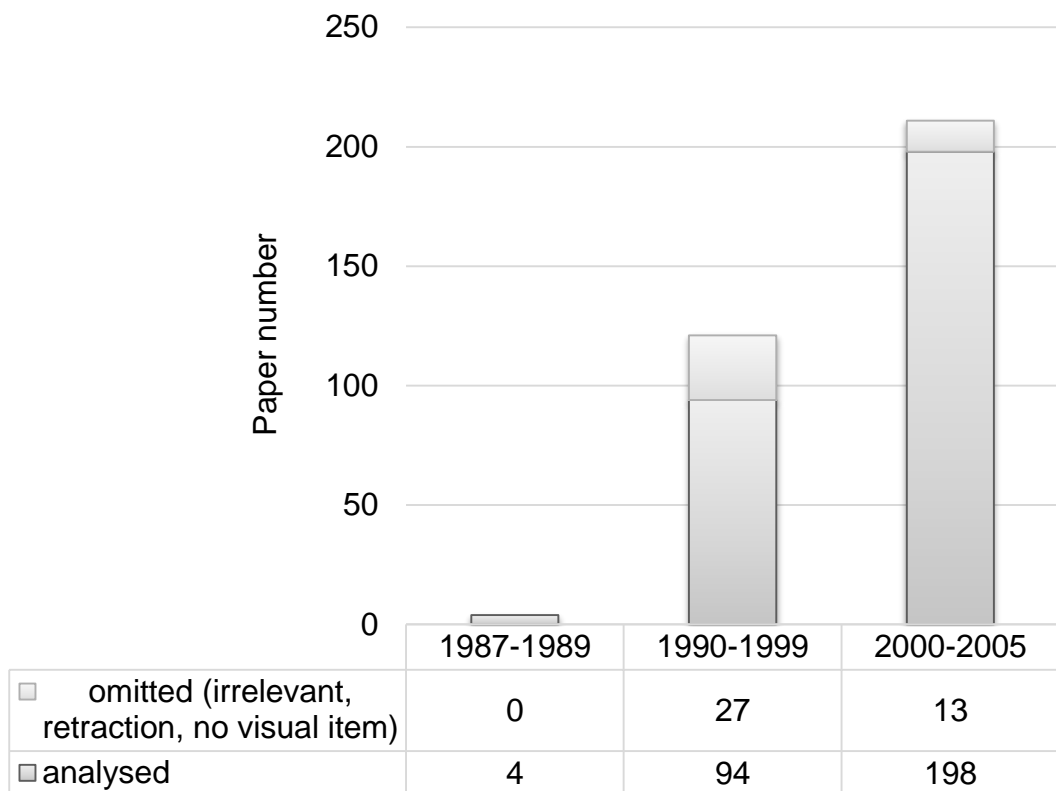
A: from Liu, Qiong A., and Michael O. Hengartner. "Candidate Adaptor Protein Ced-6 Promotes the Engulfment of Apoptotic Cells in *C. Elegans*." *Cell* 93, no. 6 (1998): 961-72, Figure 7;

B: from Ambros, Victor. "MicroRNA Pathways in Flies and Worms: Growth, Death, Fat, Stress, and Timing." *Cell* 113, no. 6 (2003): 673-76,

C: from Fisher, David E. "Apoptosis in Cancer Therapy: Crossing the Threshold." *Cell* 78, no. 4 (1994): 539-42, Figure 2.

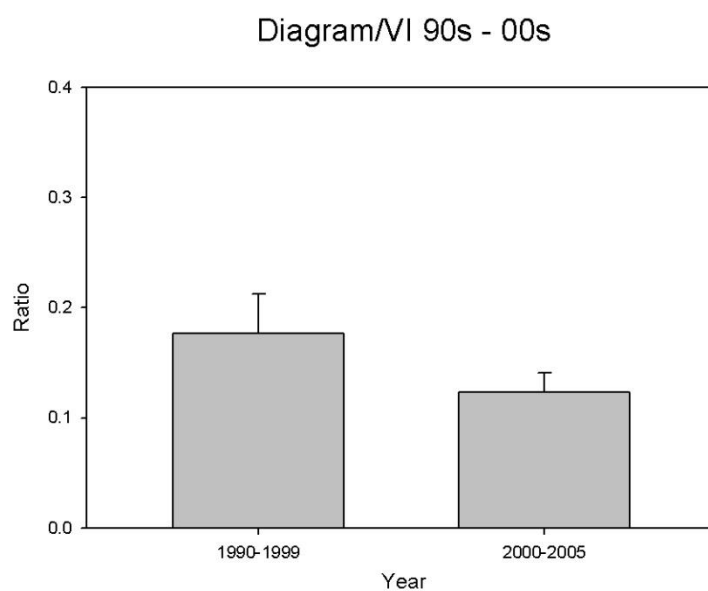


**Figure 4.2.8.1**  
Data profile of *FASEB Journal*: search results and sampled papers.



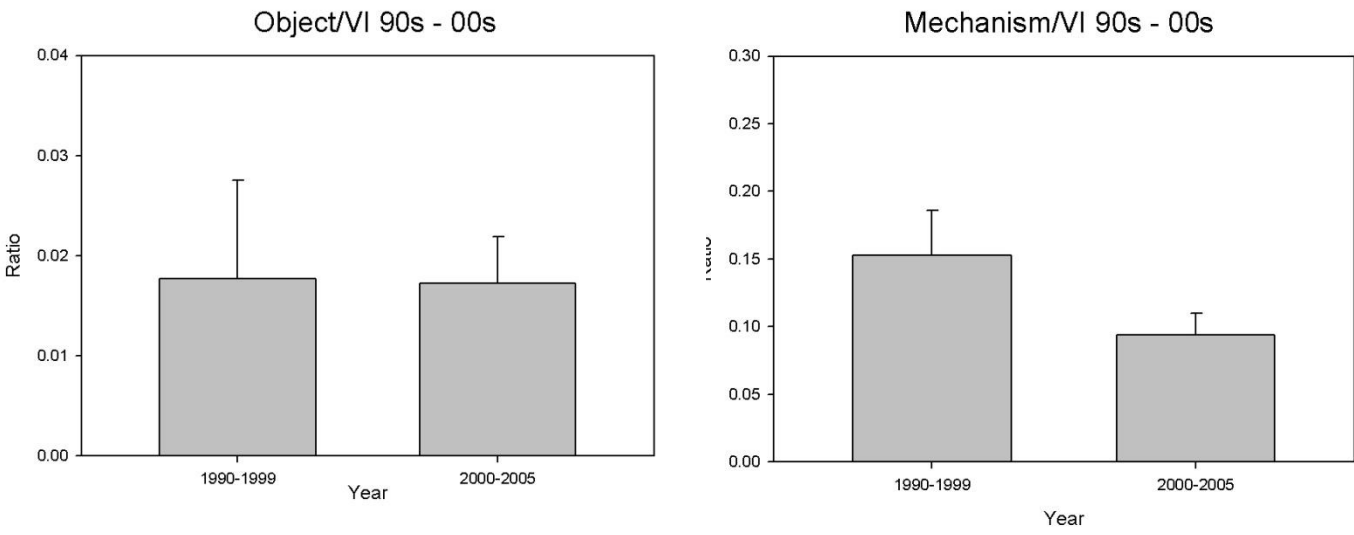
**Figure 4.2.8.2**

Data profile of *FASEB Journal*: omitted and analysed papers.

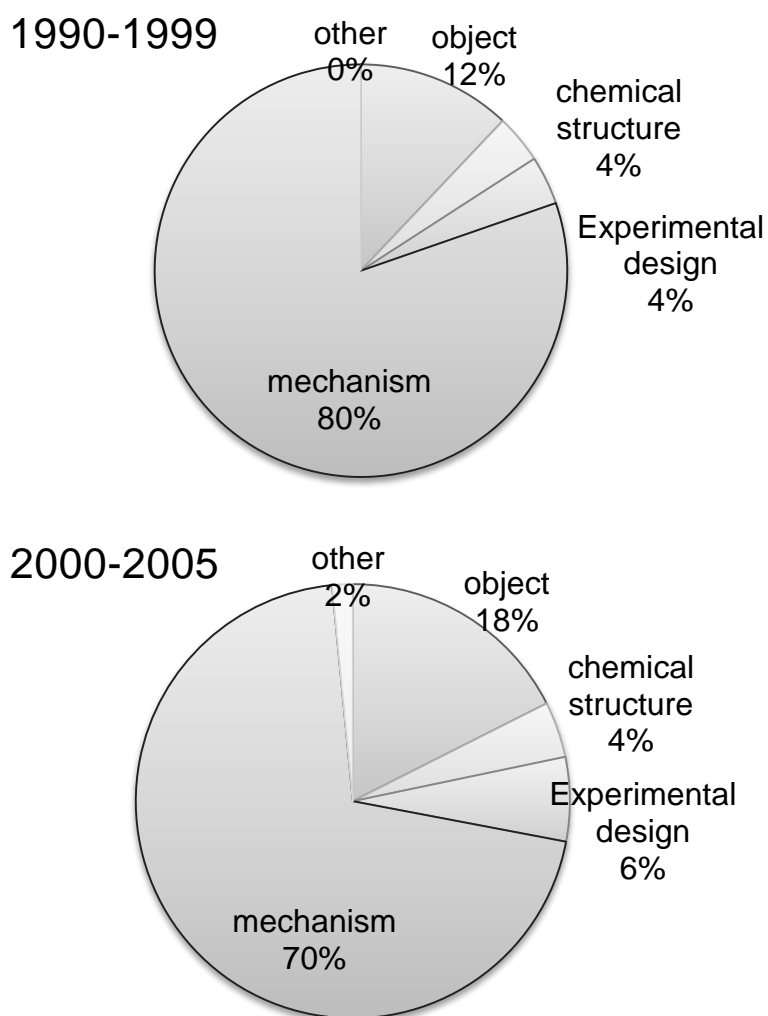


**Figure 4.2.8.3**  
D/VIs in *FASEB Journal*, 1990–2005.



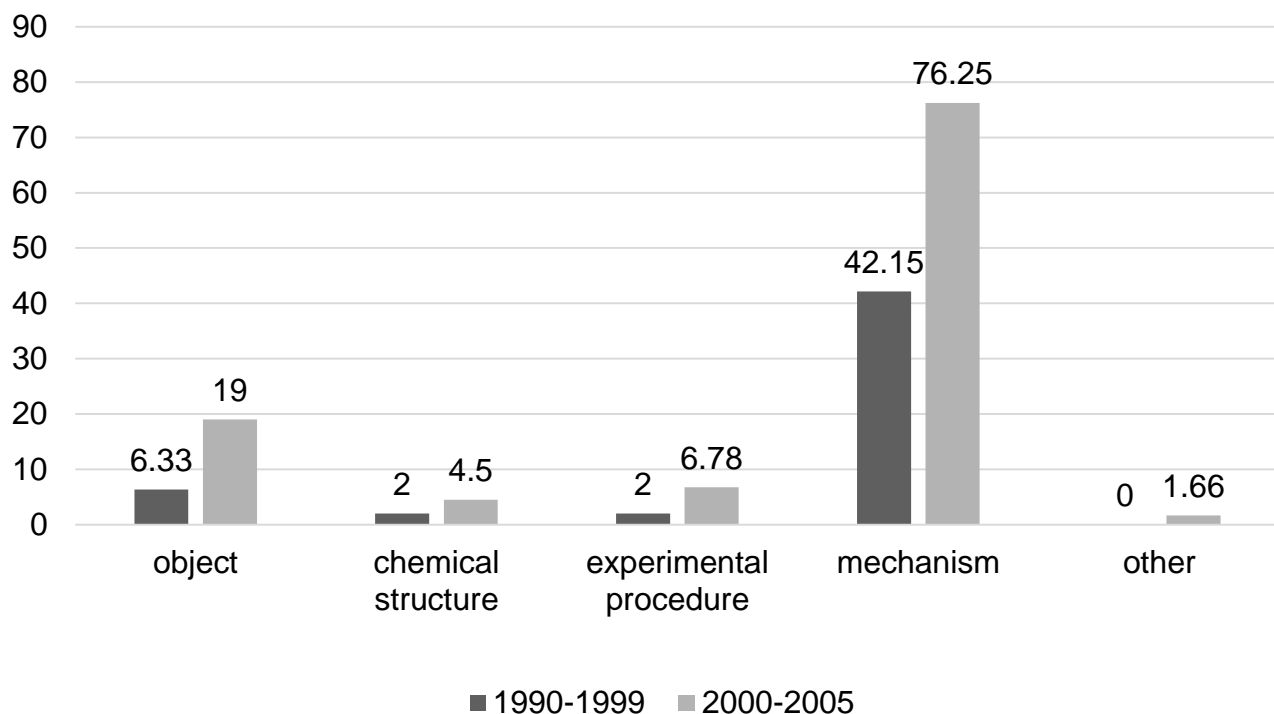


**Figure 4.2.8.4**  
D/VIs of two prevalent diagram types in *FASEB Journal*, 1990–2005.



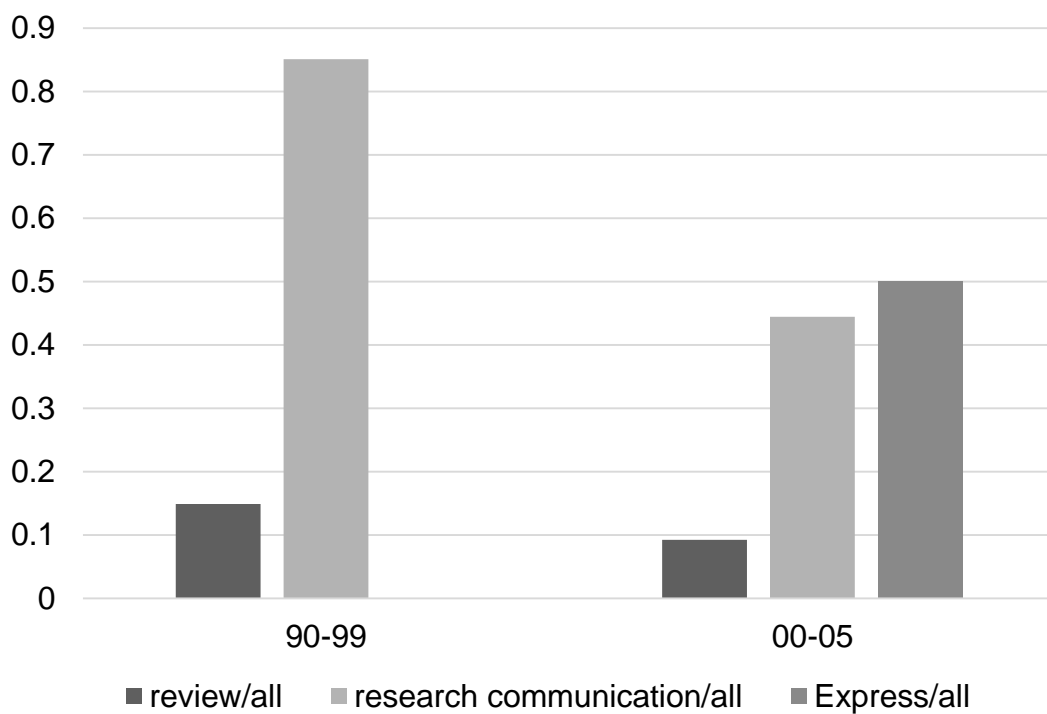
**Figure 4.2.8.5**

Proportions of five diagram types in *FASEB Journal*, 1990–2005.



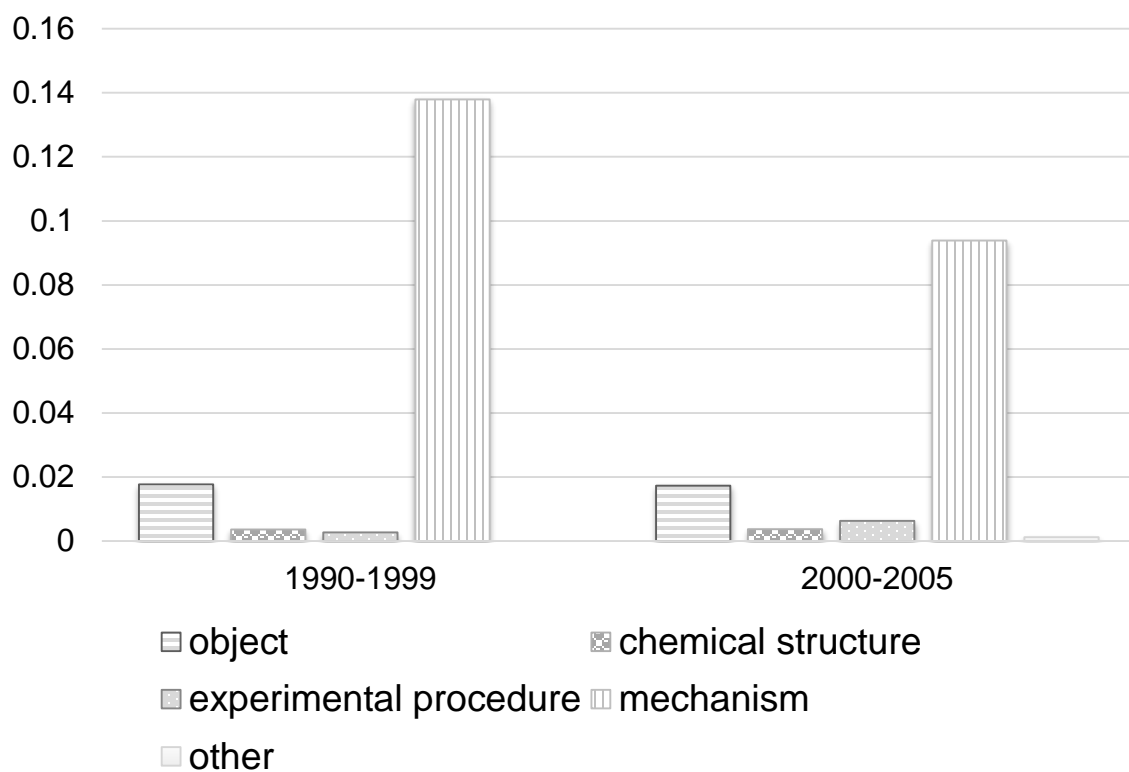
**Figure 4.2.8.6**

Number of five diagram types in *FASEB Journal*, 1990–2005.



**Figure 4.2.8.7**

Proportions of three paper categories in *FASEB Journal*, 1990–2005.



**Figure 4.2.8.8**

D/VIs of five diagram types in *FASEB Journal*, 1990–2005.



**Figure 4.2.8.9**

Object diagrams. Left: from Abdollahi, Amir, Sophie Domhan, et al. "Apoptosis Signals in Lymphoblasts Induced by Focused Ultrasound." *The FASEB Journal* (2004), Figure 1; Right: from Borlongan, Cesario V., Mitsuharu Yamamoto et al. "Glial Cell Survival Is Enhanced During Melatonin-Induced Neuroprotection against Cerebral Ischemia." *The FASEB Journal* 14, no. 10 (2000): 1307-17, Figure 7.

**Figure 4.2.8.10**

Experimental design type. From Planagum, Anna agrave, et al. "The Selective Cyclooxygenase-2 Inhibitor Sc-236 Reduces Liver Fibrosis by Mechanisms Involving Non-Parenchymal Cell Apoptosis and Ppar $\gamma$ <sup>3</sup> Activation." *The FASEB Journal* (2005), Figure 1.

**A**

**B**

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**Figure 4.2.8.11**

Experimental design type of diagrams. A: from Gitter, Alfred H., Kerstin Bendfeldt, et al. "Leaks in the Epithelial Barrier Caused by Spontaneous and TNF $\alpha$ -Induced Single-Cell Apoptosis." *The FASEB Journal* 14, no. 12 (2000): 1749-53, Figure 1;

B: from Nauenburg, Sonja, Werner Zwerschke, et al. "Induction of Apoptosis in Cervical Carcinoma Cells by Peptide Aptamers That Bind to the Hpv-16 E7 Oncoprotein." *The FASEB Journal* (2001), Figure 1.



**Figure 4.2.8.12**

“Other” type of diagram. From Suschek, Christoph V., Peter Schroeder, et al. "The Presence of Nitrite During UVA Irradiation Protects from Apoptosis." *The FASEB Journal* (2003), Figure 6.

**Figure 4.2.8.13**

“Other” type of diagram. From Jacquelin, Arnaud, Magali Herrant, et al. "Imatinib Induces Mitochondria-Dependent Apoptosis of the Bcr-Abl Positive K562 Cell Line and Its Differentiation Towards the Erythroid Lineage." *The FASEB Journal* (2003), Figure 6A.

**Figure 4.2.8.14**

“Other” type of diagram. From Pirkkala, Lila, Pävi Nykänen, et al. "Roles of the Heat Shock Transcription Factors in Regulation of the Heat Shock Response and Beyond." *The FASEB Journal* 15, no. 7 (2001): 1118-31, Figure 2B

**Figure 4.2.8.15**

“Other” type of diagram. From Unger, Roger H., and Lelio Orci. "Diseases of Liporegulation: New Perspective on Obesity and Related Disorders." *The FASEB Journal* 15, no. 2 (2001): 312-21, Figure 6A.

**A**

---

**B**

**Figure 4.2.8.16**

Mechanism diagrams. A: from Hamel, P. A., R. A. Phillips, et al. "Speculations on the Roles of Rb1 in Tissue-Specific Differentiation, Tumor Initiation, and Tumor Progression." *The FASEB Journal* 7, no. 10 (1993): 846-54, Figure 1; B: from Tosetti, Francesca, Nicoletta Ferrari, et al. "'Angioprevention': Angiogenesis Is a Common and Key Target for Cancer Chemopreventive Agents." *The FASEB Journal* 16, no. 1 (2002): 2-14, Figure 1.

**Figure 4.2.8.17**

Mechanism diagram. From Planagum et al. "The selective cyclooxygenase-2 inhibitor SC-236 reduces liver fibrosis by mechanisms involving non-parenchymal cell apoptosis and PPAR $\gamma$  activation." *The FASEB Journal*, (2005), Figure 9.

**Figure 4.2.8.18**

Mechanism diagram. From Davies, Sean S., Venkataraman Amarnath, et al. "Effects of Reactive G-Ketoaldehydes Formed by the Isoprostane Pathway (Isoketals) and Cyclooxygenase Pathway (Levuglandins) on Proteasome Function." *The FASEB Journal* (2002), Figure 1.

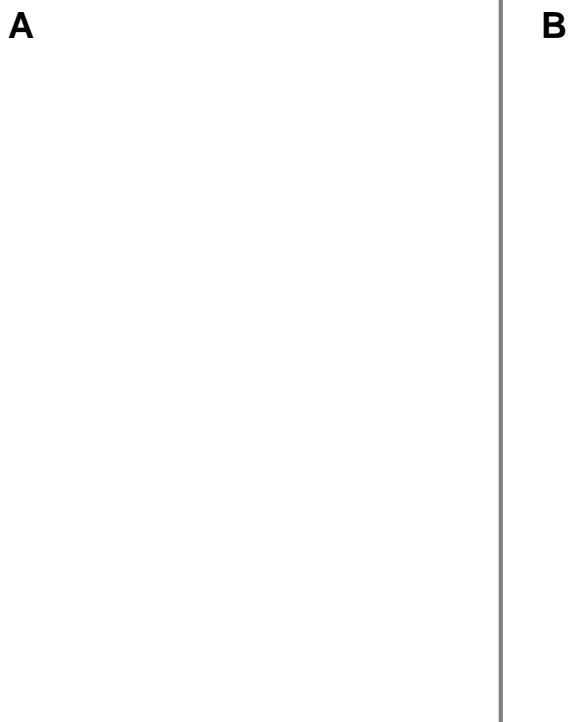
**A**

**B**

**Figure 4.2.8.19**

A: Mechanism diagram. From Lynn, W. S., and P. K. Wong. "Neuroimmunodegeneration: Do Neurons and T Cells Use Common Pathways for Cell Death?" *The FASEB Journal* 9, no. 12 (1995): 1147-56, figure2; B: "other" type of diagram, from Wang, Eugenia. "Age-Dependent Atrophy and Microgravity Travel: What Do They Have in Common?" *The FASEB Journal* 13, no. 9001 (1999): 167-74, Figure 1.





**Figure 4.2.8.20**

Mechanism diagrams. A: from Garrido, Carmen, Jean-Marie Bruey, et al. "Hsp27 Inhibits Cytochrome C-Dependent Activation of Procaspase-9." *The FASEB Journal* 13, no. 14 (1999): 2061-70, Figure 10;

B: from Cadet, Jean Lud, Subramaniam Jayanthi, et al. "Speed Kills: Cellular and Molecular Bases of Methamphetamine-Induced Nerve Terminal Degeneration and Neuronal Apoptosis." *The FASEB Journal* 17, no. 13 (2003): 1775-88, Figure 3.

**Figure 4.2.8.21**

Mechanism diagram. From Savaskan, Nicolai E., Anja U. Bräuer, et al. "Selenium Deficiency Increases Susceptibility to Glutamate-Induced Excitotoxicity." *The FASEB Journal* (2002), Figure 7.

**Figure 4.2.8.22**

Mechanism diagram. From Fadeel, Bengt, Boris Zhivotovsky, et al. "All Along the Watchtower: On the Regulation of Apoptosis Regulators." *The FASEB Journal* 13, no. 13 (1999): 1647-57, Figure 1.

**Figure 4.2.8.23**

Mechanism diagram. From Luciano, Frederic, Magali Herrant, et al. "The P54-Cleaved Form of the Tyrosine Kinase Lyn Generated by Caspases During Bcr-Induced Cell Death in B Lymphoma Acts as a Negative Regulator of Apoptosis." *The FASEB Journal* (2003), Figure 8.

**A**

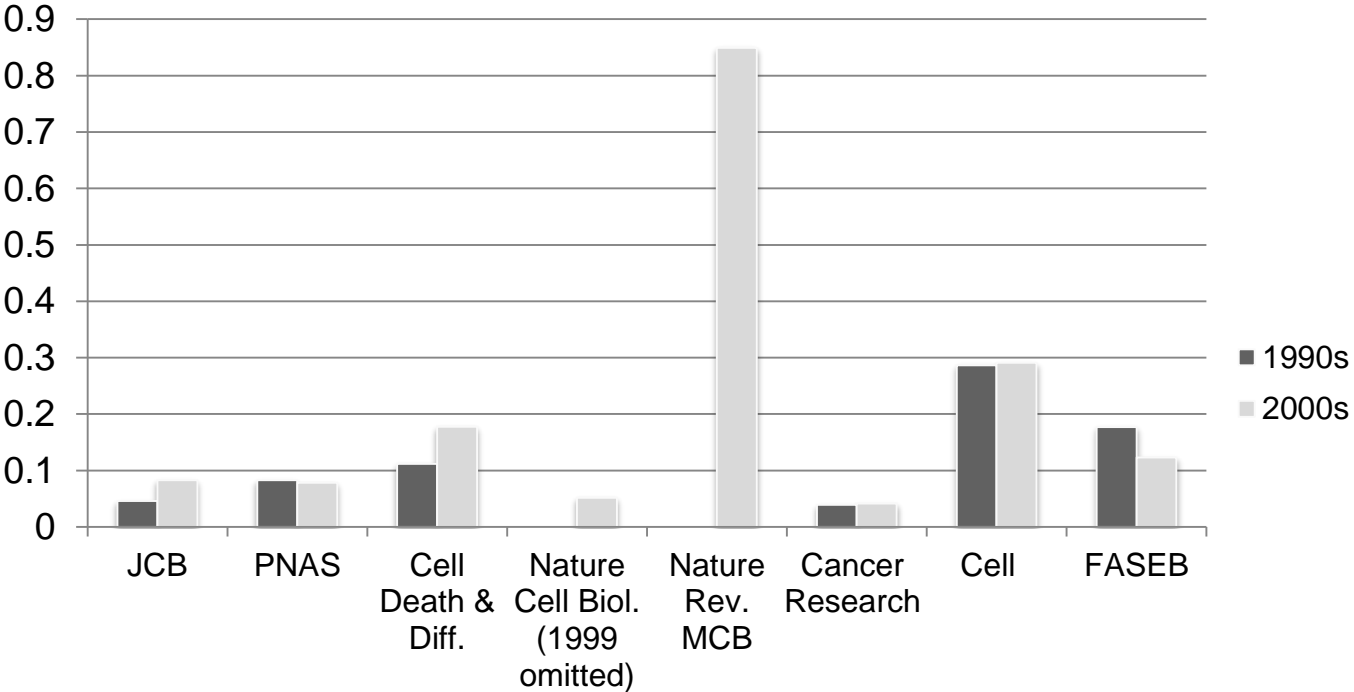
**B**

**Figure 4.2.8.24**

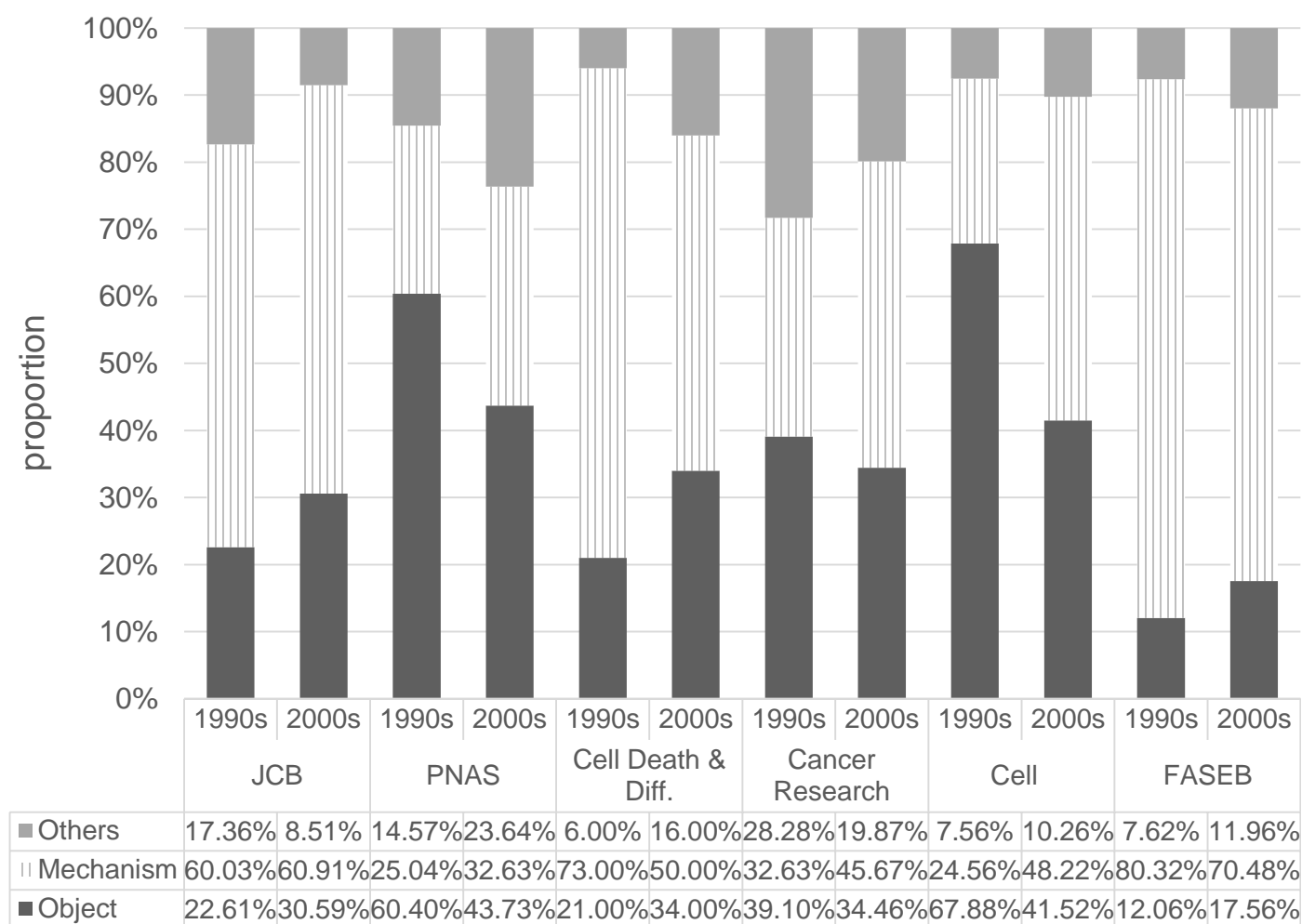
Mechanism diagrams. A: from Spiegel, S., and A. H. Merrill. "Sphingolipid Metabolism and Cell Growth Regulation." *The FASEB Journal* 10, no. 12 (1996): 1388-97, Figure 3;  
B: from Santella, L., and E. Carafoli. "Calcium Signaling in the Cell Nucleus." *The FASEB Journal* 11, no. 13 (1997): 1091-109, Figure 1.

**Figure 4.2.8.25**

Mechanism diagram. From Unger et al. (2001), Figure 2.



**Figure 5.1**  
Overview of D/VIs in all journals surveyed, 1990s and 2000s.



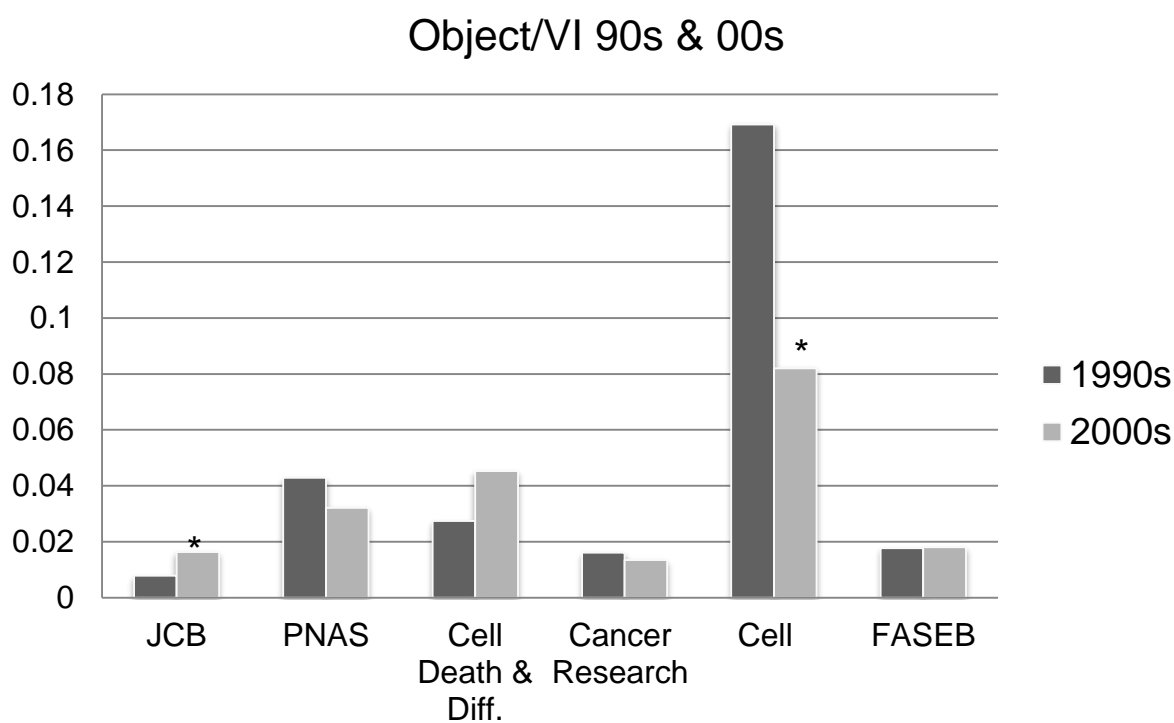
**Figure 5.2**

Overview of proportions of different diagram types in six of journals surveyed, 1990s and 2000s.

Note: “Others” = chemical structure + experimental design + other (miscellaneous)

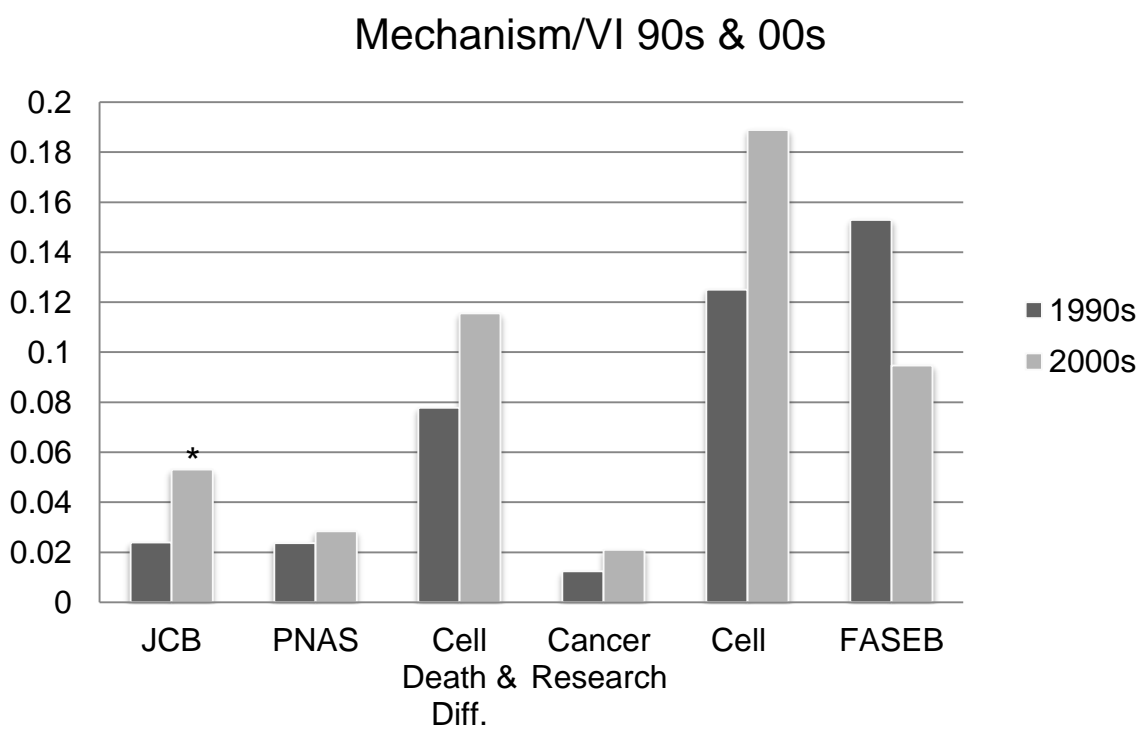
This chart provides comparisons of proportions both between the types and across journals.





**Figure 5.3**

D/VIs of object diagrams in six surveyed journals, 1990s and 2000s.



**Figure 5.4**

D/VIs of mechanism diagrams in six journals, 1990s and 2000s.

**A**

**B**

**C**

**Figure 5.5**

Example object diagrams of visual resemblance: microscopic observations and/or photographs. A: as cited in Fig. 4.2.1.7; B: as cited in Fig. 4.2.1.8; C: as cited in Fig. 4.2.2.8

**Figure 5.6**

Example diagram (experimental design type) of visual resemblance: experimental settings.  
From: as cited in Fig. 4.2.8.11.

**A**

**B**

**Figure 5.7**

Example object diagrams that are visually similar to calligram/graphic poetry.  
A: as cited in Fig. 4.2.1.9; B: as cited in Fig. 4.2.6.16.

**Figure 5.8**

Example object diagrams: containing symbolic and imaginary elements.  
From: as cited in Fig. 4.2.2.5.

**A**

**B**

**Figure 5.9**

Example mechanism diagrams: containing symbolic and imaginary elements.  
A: as cited in Fig. 4.2.5.11B; B: as cited in Fig. 4.2.6.22.



**Figure 5.10**

Modular use of visual elements. Left: as cited in Fig. 4.2.1.21; right: as cited in fig. 4.2.2.23.  
The right set of diagrams appear in different figures in the original paper.





**Figure 5.11**

Modular use of visual elements. From: as cited in Fig. 4.2.7.15.  
These diagrams appear in different figures in the original paper. .



**Figure 5.12**

Elements from non-specialist areas (1): facial expression icons. A: as cited in Figure 4.2.2.14; B: as cited in Figure 4.2.7.29; C: as cited in Figure 4.2.6.35.

**A**

**B**

**Figure 5.13**

Elements from non-specialist areas (2): metaphorical scissors. A: as cited in Figure 4.2.3.14; B: as cited in Figure 4.2.8.23.

**A**

**B**

**C**

**Figure 5.14**

Elements from non-specialist areas (3): death signs. A: as cited in Figure 4.2.5.10B;  
B: as cited in Figure 4.2.6.36; C: as cited in Figure 4.2.1.15.

**A**

**B**

**Figure 5.15**

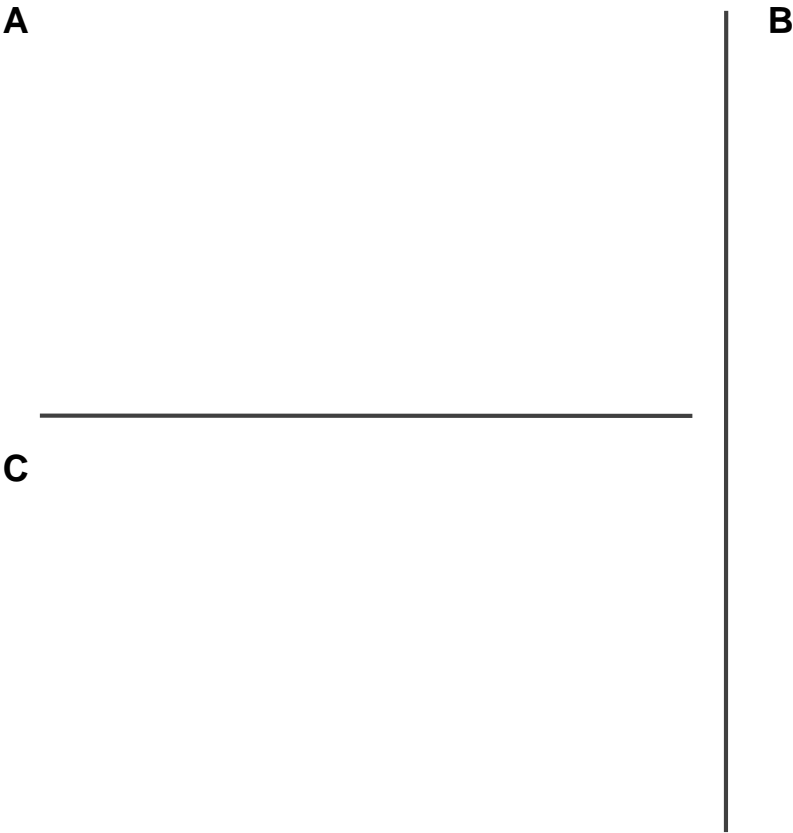
Elements from non-specialist areas (4): analogies. A: as cited in Figure 4.2.4.10;  
B: as cited in Figure 4.2.7.29.

**A**

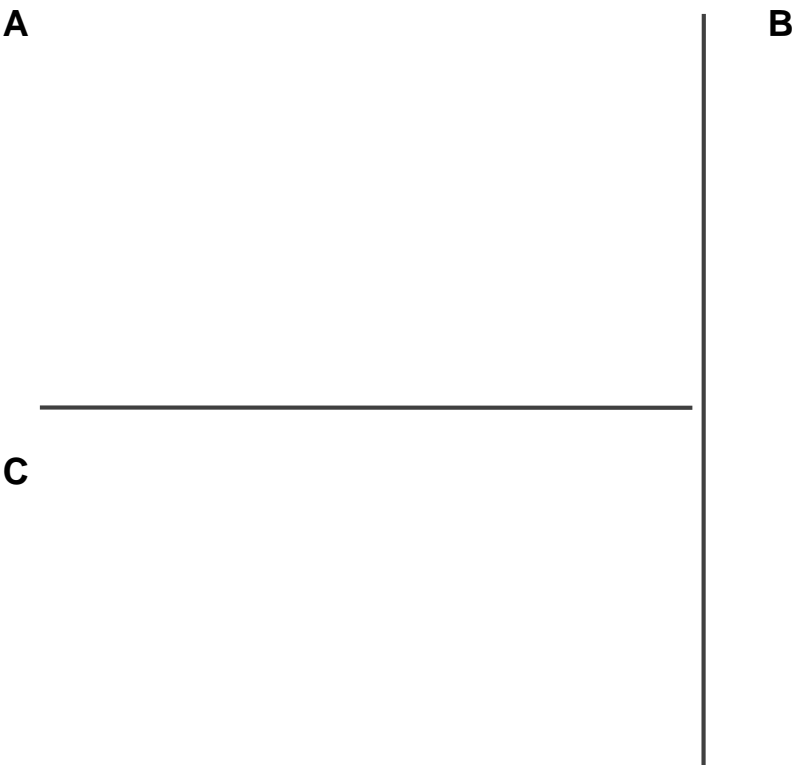
**B**

**Figure 5.16**

Plural meanings of visual elements (arrows). A: as cited in Figure 4.2.7.24C; B: as cited in Figure 4.2.2.16.



**Figure 5.17**  
Specifically-designed icons: mitochondria as a typical example. A: as cited in Figure 4.2.6.25; B: as cited in Figure 4.2.3.11; C: as cited in Figure 4.2.5.10A.

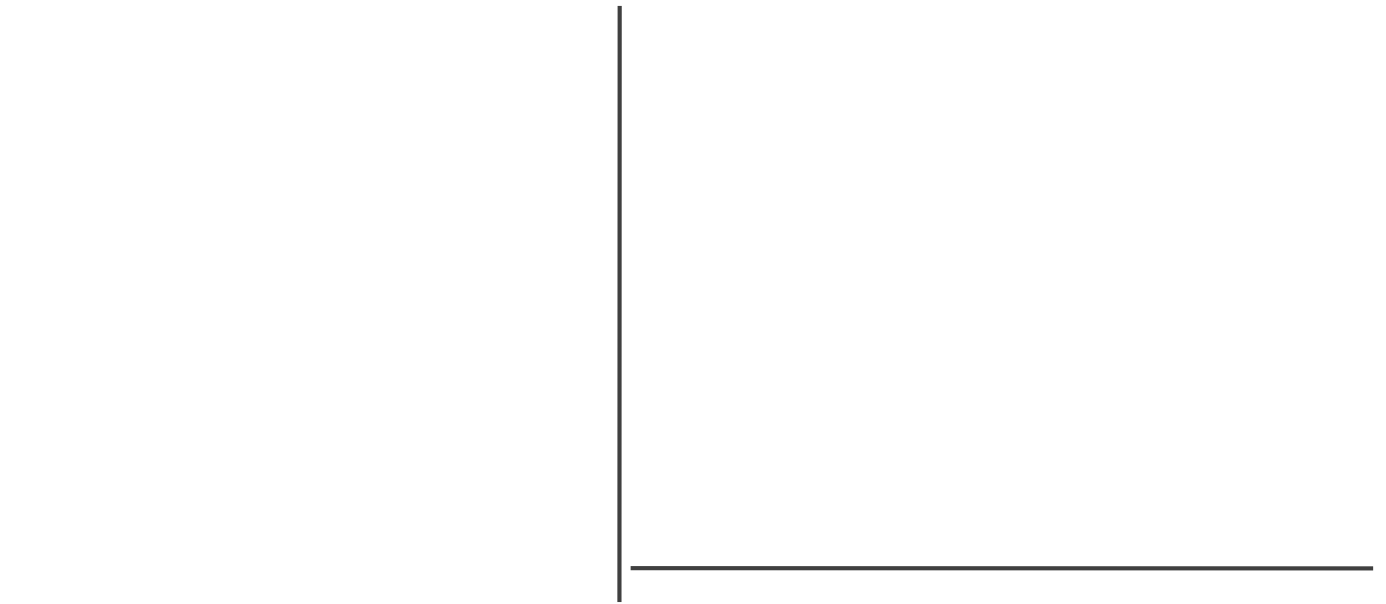


**Figure 5.18**

Examples of especially figurative mitochondria icons compared to other component elements. Diagrams that have not been cited in Chapter Four were selected to show the popularity of such a case.

A: from Zhou, Honglin, Xin-Ming Li, Judy Meinkoth, and Randall N. Pittman. "Akt Regulates Cell Survival and Apoptosis at a Postmitochondrial Level." *The Journal of Cell Biology* 151, no. 3 (2000): 483-94, Figure 10; B: from Janssens, Sophie, Antoine Tinel, Saskia Lippens, and Jürg Tschopp. "PIDD Mediates NF- $\kappa$ B Activation in Response to DNA Damage." *Cell* 123, no. 6 (2005): 1079-92, Figure 7; C: from Budd, Samantha L., Lalitha Tenneti, Timothy Lishnak, and Stuart A. Lipton. "Mitochondrial and Extramitochondrial Apoptotic Signaling Pathways in Cerebrocortical Neurons." *PNAS* 97, no. 11 (2000): 6161-66, Figure 5e.





### Figure 5.19

Diagrams of protein structures made by computer programmes.  
Upper left: from Brunet, Anne, Fumihiko Kanai, Michael B. Yaffe et al., "14-3-3 Transits to the Nucleus and Participates in Dynamic Nucleocytoplasmic Transport." *The Journal of Cell Biology* 156, no. 5 (2002): 817-28, Figure 4A;  
upper right: from Chami, Mounia, Devrim Gozuacik, Patrizia Paterlini-Bréchet et al., "Serca1 Truncated Proteins Unable to Pump Calcium Reduce the Endoplasmic Reticulum Calcium Concentration and Induce Apoptosis." *The Journal of Cell Biology* 153, no. 6 (2001): 1301-14, Figure 1C;  
lower: as cited in Figure 4.2.5.5B.

**Figure 5.20**

Early diagrams of protein structures (1). From Richardson, Jane S. "Early Ribbon Drawings of Proteins." *Nature Structural Biology* 7 (2000): 624-25, Figure 1.

**A**

**B**

**Figure 5.21**

Early diagrams of protein structures (2). A: from Hubbard, Ruth, and Allen Kropf. "Molecular Isomers in Vision." *Scientific American* June 1967, 260-69, 261; B: from Dickerson, Richard D. "The Structure and History of an Ancient Protein." *Scientific American* April 1972, 82-95, 88; C: from Neurath, Hans. "Protein-Digesting Enzymes." *Scientific American* December 1964, 248-59, 256.

**C**

**Figure 5.22**

Early diagrams of protein structures (3). From Phillips, David C. "The Three-Dimensional Structure of an Enzyme Molecule." *Scientific American* November 1966, 62-74, 68-69.

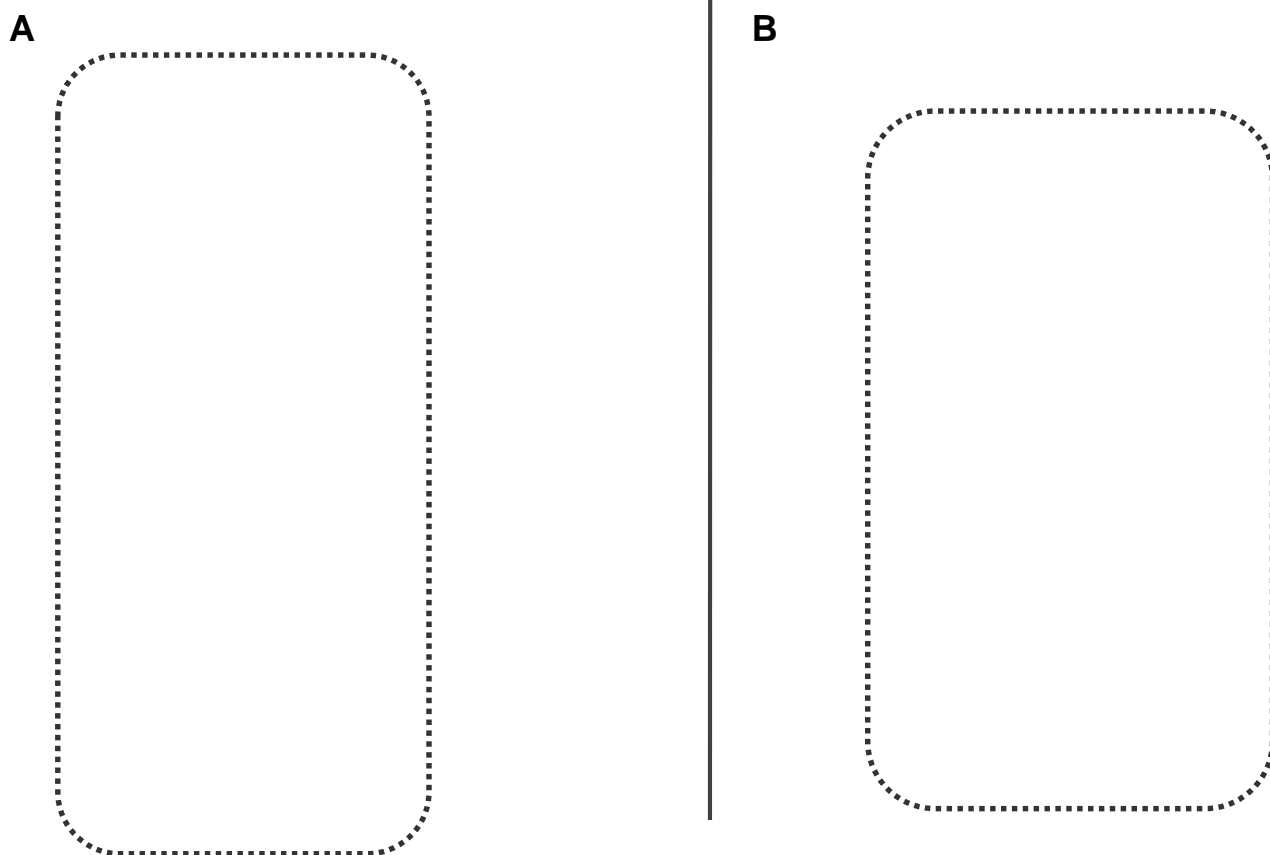
**A**

---

**B**

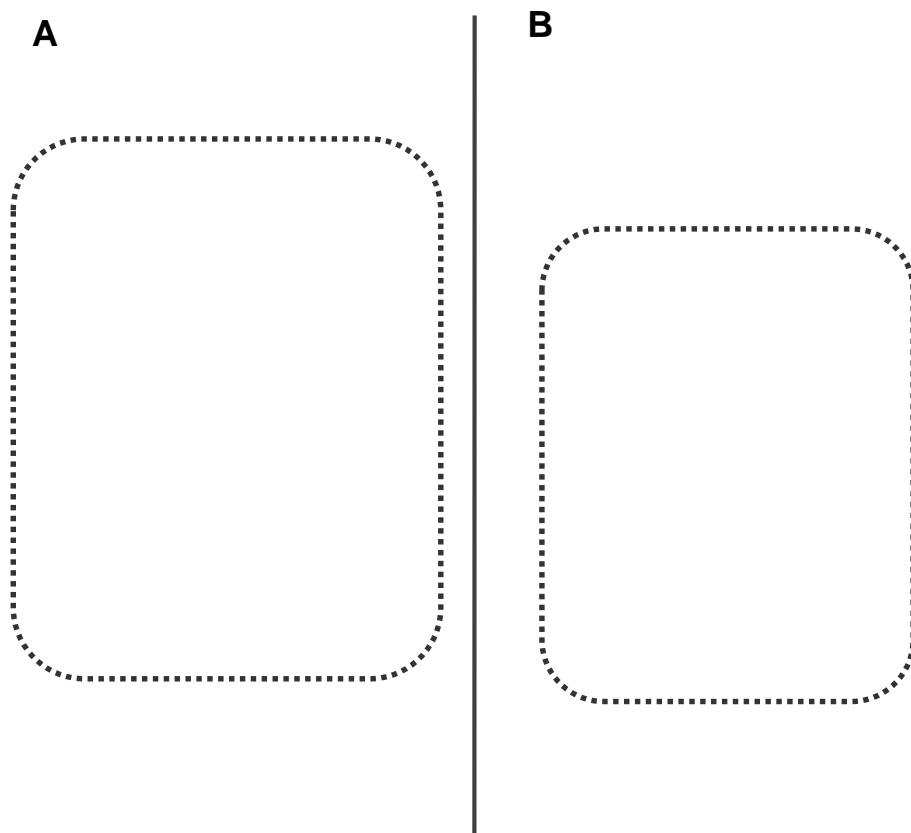
**Figure 5.23**

Diagrams embedding representations of protein structures. A: as cited in Figure 4.2.2.22;  
B: as cited in Figure 4.2.2.7.



**Figure 5.24**

Mechanism diagrams: advanced artistic tools and traditional style (1). Note the areas framed with dotted outlines. They present the nearly same pathways. A: as cited in Figure 4.2.7.25; B: as cited in Figure 4.2.3.11 (also used as Figure 5.17B).



**Figure 5.25**

Mechanism diagrams: advanced artistic tools and traditional style (2). Note the areas framed with dotted outlines. They present the nearly same pathways (also nearly the same with those two in Figure 5.21). A: as cited in Figure 4.2.6.32; B: as cited in Figure 4.2.5.11B (also used as Figure 5.9A).

**Figure 5.26**

Mechanism diagrams: advanced artistic tools and traditional style (3). From: as cited in Figure 4.2.8.17.



**Figure 5.27**

A mechanism diagram synthesising heterogeneous information from two disciplines.  
From: as cited in Figure 4.2.6.27.

**Figure 5.28**

This mechanism diagram synthesises discoveries from different practices.  
From: as cited in Figure 4.2.2.17.

**A**

**B**

---

**Figure 5.29**

A is a mechanism diagram synthesising heterogeneous information within a cohesive, uniform system of elements. B contains diverse styles of elements. From: as cited in Figure 4.2.2.24.

**Figure 5.30**

Example of mechanism diagram synthesising data image and drawing of model (1). From: as cited in Figure 4.2.6.28.

**Figure 5.31**

Example of mechanism diagram  
synthesising data image and  
drawing of model (2). From: as  
cited in Figure 4.2.7.28.

**Figure 5.32**

This mechanism diagram synthesises heterogeneous perspectives. From: as cited in Figure 4.2.2.19.

**A**

---

**B**

**Figure 5.33**

These two mechanism diagrams synthesise different parts of research process and heterogeneous perspectives. A: as cited in Figure 4.2.1.17; B: as cited in Figure 4.2.6.30.